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(54) Title: NOVEL BONE MARROW NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel bone marrow expressed nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof.

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## NOVEL BONE MARROW NUCLEIC ACIDS AND POLYPEPTIDES

### 1. BACKGROUND OF THE INVENTION

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#### 1.1 TECHNICAL FIELD

The present invention provides novel bone marrow-expressed polynucleotides and bone marrow-expressed proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research  
10 methods.

#### 1.2 BACKGROUND

Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs, chemokines, and interleukins) has matured  
15 rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal  
20 sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the  
25 case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

The bone marrow is a well-organized tissue located within the central cavity of bone. It has a complex three-dimensional structure that is richly innervated and highly  
30 vascularized. Two primary cell types make up the structure of the bone marrow. These are the stromal, and parenchymal cells. Stromal cells include reticular cells such as



fibroblasts, endothelial cells, adipocytes, as well as cells of the osteochondrogenic lineage. They exert important influences on osteoclastogenesis and lymphopoiesis, and have additional effects on bone turnover. Parenchymal cells are comprised of the hematopoietic cells, and are important for proliferation, maturation, and migration of  
5 cells that make up the blood.

In the adult, hematopoiesis takes place primarily in the bone marrow. Therefore, all of the cells that make up the blood, such as erythrocytes, platelets, basophils, natural killer cells, eosinophils, T- and B-lymphocytes, neutrophils, macrophages, and others, are produced in this structure. Each of these cells is derived from a common, self-renewing  
10 stem cell that proliferates, and/or differentiates depending on regulatory molecules that are produced by the stromal cells. Stromal cells are predominantly a mixture of fibroblasts, macrophage/dendritic lineage cells, epithelial cells, and endothelial cells. They influence the fate of hematopoietic cells through the secretion of soluble factors, cytokines, and the expression of membrane-anchored growth factors, and cell surface  
15 recognition molecules.

Cytokines are necessary for normal hematopoiesis in the bone marrow, and provide a means of fine-tuning bone marrow function in response to stimulation. They are not only produced by stromal cells, but can also be secreted by macrophages, and antigen-stimulated T lymphocytes for the purpose of replenishing leukocytes that may be  
20 consumed during immune and inflammatory reactions. Many cytokines that influence the differentiation and expansion of hematopoietic progenitor cells are termed colony-stimulating factors, because they were initially assayed by their ability to stimulate the formation of cell colonies in bone marrow cultures. Some of these colony-stimulating factors (CSFs) include, granulocyte-CSF, granulocyte/macrophage-CSF, monocyte-CSF,  
25 Kit-ligand, interleukin (IL)-6, FLK-2 ligand, and leukemia inhibitory factor. Each of these stimulates the growth and development of various leukocytic or erythroid colonies. Other cytokines secreted in the bone marrow include IL-9, a T cell line and mast cell progenitor-stimulating factor, IL-11, a megakaryocytopoiesis stimulator, and IL-7, a cytokine that influences the survival and expansion of immature precursors committed to  
30 the B and T cell lineages. Many other cytokines are also secreted in the bone marrow.

Cell-surface molecules that represent several adhesion molecule superfamilies including integrins, selectins, sialomucins and the immunoglobulin domain-containing proteins, are important in supporting cell-cell and cell-extracellular matrix interactions in the bone marrow. These proteins are critical to the homing of progenitor cells selectively to the marrow stroma for proliferation and differentiation. They also serve to influence the fate of the progenitor cells by directing them to differentiate into a specific lineage. For example, VLA-4 directs control of late erythroid differentiation and pro-B cell maturation.

The bone marrow is also the site of B cell development. B cells begin as lymphoid stem cells that differentiate into progenitor B-cells, or pro-B cells. Pro-B cells proliferate within the bone marrow, and fill the extravascular spaces between large sinusoids in the shaft of the bone. They next mature into precursor B cells, pre-B cells. The stromal cells of the bone marrow are crucial for both pro- and pre-B cell development because they provide a source of cytokines, and a substrate for direct interaction with the pro- and pre-B cells. Pro-B cells require interaction with VCAM-1 and stem-cell factor (SCF) on the stromal cells to induce expression of the IL-7 receptor. Secretion of IL-7 by the stromal cells then induces the pro-B cells to mature into pre-B cells. Continued IL-7 secretion by stromal cells induces pre-B cells to begin proliferating and eventually differentiates them into immature B-cells. In addition, a selection process within the bone marrow eliminates B cells with self-reactive phenotypes, functioning to protect against autoimmune disease.

The bone marrow environment also influences bone turnover and bone precursor cell functions. Bone marrow stromal cells include the precursors of the osteochondrogenic lineage, and can modulate the effects of some systemic factors on bone turnover. Furthermore, hematopoietic cells may influence the differentiation of osteogenic cells, and mature lymphocytes may impact osteoclastic and osteoblastic functions. For instance, B-lymphocytes have been implicated in the secretion of factors that change the immunological milieu at sites of new bone induction and influence new bone formation.

The identified bone marrow-expressed polynucleotide and polypeptide sequences may have applications in hematopoiesis, stem cell survival, and bone growth and

remodeling. Identification of secreted factors that stimulate hematopoiesis may serve to produce greater immune responses in immunosuppressed individuals. The identification of factors that preferentially stimulate specific hematopoietic cell types may also allow the prevention of specific disorders such as anemia in the case erythroid cell stimulating factors, or platelet deficiency in the case of megakaryocyte stimulating factors. Likewise, stem cell stimulating factors may be used to restore blood cell populations following chemotherapy treatments for cancer. Therapy to stimulate bone healing and remodeling may also be identified by the discovery of novel factors in the bone marrow that influence bone resorption by osteoclasts, or new bone cell differentiation from stromal cells.

## 2. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides from bone marrow tissue, and novel isolated polynucleotides from bone marrow tissue encoding such polypeptides, including recombinant DNA molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-113, 227-339 and 453-477 and are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenine; C is cytosine; G is guanosine; T is

thymine; and N is any of the four bases. In the amino acids provided in the Sequence Listing, \* corresponds to the stop codon.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO: 1 –113, 227 – 339 or 453-477 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO: 1 –113, 227 – 339 or 453-477. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO: 1 –113, 227 – 339 or 453-477 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1 –113, 227 – 339 or 453-477. The sequence information can be a segment of any one of SEQ ID NO: 1 –113, 227 – 339 or 453-477 that uniquely identifies or represents the sequence information of SEQ ID NO: 1 –113, 227 – 339 or 453-477.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information are provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing full-length genes, use for

chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

In a preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1 – 113, 227-339 or 453-477, or novel segments or parts of the nucleic acids of the invention are used as  
5 primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1 – 113, 227 – 339 or 453 – 477 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying bone marrow tissues and cells; for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed  
10 sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO: 1 – 113, 227 – 339 and 453-477; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO: 1 – 113, 227 – 339 and 453-477; and a polynucleotide  
15 comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1 – 113, 227 – 339 and 453-477. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO: 1 – 113, 227 – 339 and 453-477; (b) a nucleotide sequence encoding any one of the  
20 amino acid sequences comprising SEQ ID NO: 114 – 226, 340 – 452 and 478-502; (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (e.g. orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set  
25 forth in the Sequence Listing.

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in the Sequence Listing; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the  
30 polynucleotides having a nucleotide sequence set forth in SEQ ID NO: 1 – 113, 227 – 339 and 453-477; or (b) polynucleotides that hybridize to the complement of the polynucleotides

of (a) under stringent hybridization conditions, or (c) polypeptides comprising any of the polypeptide sequences set forth in SEQ ID NO: 114 – 226, 340 – 452 and 478-502.

Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and “substantial equivalents” thereof (e.g., with at least about 65%, 70%,  
5 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably produced by recombinant means using the genetically engineered cells (e.g. host cells) of the invention. The polypeptides may have the initial methionine (Met) removed.

10 The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, e.g., pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

15 The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

20 Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein, and use in generation of anti-sense DNA or RNA, their chemical analogs and the like.

25 For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, *e.g.*, *in situ* hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as  
30 expressed sequence tags for identifying expressed genes or, as well known in the art and

exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of

the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (i.e., increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other substances that interact with (*e.g.*, bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound the binds to a polypeptide of the invention is identified.

The methods of the invention also provide methods for treatment that involve the administration of the polynucleotides or polypeptides of the invention to individuals exhibiting symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can affect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in Tables 1A-D and 7); for which they have a signature region (as set forth in Table 2 and 8); or for which they have homology to a gene family (as set forth in Table 3). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in increasing hematopoiesis, stem cell survival, and bone growth and remodeling.



### 3. DETAILED DESCRIPTION OF THE INVENTION

#### 3.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular  
5 forms "a", "an" and "the" include plural references unless the context clearly dictates  
otherwise.

The term "active" refers to those forms of the polypeptide that retain the biologic  
and/or immunologic activities of any naturally occurring polypeptide. According to the  
invention, the terms "biologically active" or "biological activity" refer to a protein or  
10 peptide having structural, regulatory or biochemical functions of a naturally occurring  
molecule. Likewise "immunologically active" or "immunological activity" refers to the  
capability of the natural, recombinant or synthetic polypeptide to induce a specific  
immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells" as used in this application are those cells which are  
15 engaged in extracellular or intracellular membrane trafficking, including the export of  
secretory or enzymatic molecules as part of a normal or disease process.

The terms "complementary" or "complementarity" refer to the natural binding of  
polynucleotides by base pairing. For example, the sequence 5'-AGT-3' binds to the  
complementary sequence 3'-TCA-5'. Complementarity between two single-stranded  
20 molecules may be "partial" such that only some of the nucleic acids bind or it may be  
"complete" such that total complementarity exists between the single stranded molecules.  
The degree of complementarity between the nucleic acid strands has significant effects on  
the efficiency and strength of the hybridization between the nucleic acid strands.

The term "embryonic stem cells (ES)" refers to a cell that can give rise to many  
25 differentiated cell types in an embryo or an adult, including the germ cells. The term  
"germ line stem cells (GSCs)" refers to stem cells derived from primordial stem cells that  
provide a steady and continuous source of germ cells for the production of gametes. The  
term "primordial germ cells (PGCs)" refers to a small population of cells set aside from  
other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during  
30 embryogenesis that have the potential to differentiate into germ cells and other cells.  
PGCs are the source from which GSCs and ES cells are derived. The PGCs, the GSCs

and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides  
5 that modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs is nucleic acid fragments that induce  
10 the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonucleotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic  
15 or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of  
20 the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion,"  
25 or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 9 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides,  
30 more preferably less than about 100 nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from

about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can be used in polymerase chain reaction (PCR), various hybridization procedures or microarray procedures to identify or  
5 amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEQ ID NOs: 1-113, 227-339, and 453-477.

Probes may, for example, be used to determine whether specific mRNA  
10 molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A  
15 Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NOs: 1-113, 227-339, or 453-  
20 477. The sequence information can be a segment of any one of SEQ ID NOs: 1-113, 227-339, or 453-477 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO: 1-113, 227-339, or 453-477. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion  
25 base pairs in one set of chromosomes. Because  $4^{20}$  possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosome. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteen-mer segments can be used. The probability that the fifteen-  
30 mer is fully matched in the expressed sequences is also approximately one in five because

expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match ( $1/4^{25}$ ) times the increased probability for mismatch at each nucleotide position (3 x 25). The probability that an eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

The terms "operably linked" or "operably associated" refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements e.g. repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term "pluripotent" refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

The terms "polypeptide" or "peptide" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 200 amino acids, more preferably less than 150 amino acids and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200

amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term "translated protein coding portion" means a sequence that encodes for the full-length protein which may include any leader sequence or any processing sequence.

The term "mature protein coding sequence" means a sequence that encodes a peptide or protein without a signal or leader sequence. The "mature protein portion" means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell that removes any leader/signal sequence. The mature protein portion may or may not include an initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (e.g., with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant" (or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, e.g., recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes that produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression  
5 in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

10 Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example,  
15 nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably  
20 in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

Alternatively, where alteration of function is desired, insertions, deletions or  
25 non-conservative alterations can be engineered to produce altered polypeptides. Such alterations can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate  
30 polypeptides that are better suited for expression, scale up and the like in the host cells

chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, *e.g.*, polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 Daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (*e.g.*, nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (*e.g.*, yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use in yeast or eukaryotic expression

systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells that have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells that have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g., receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (e.g. Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2):134-143) and factors released from damaged cells (e.g. Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.



The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (i.e., hybridization to filter-bound DNA in 0.5 M NaHPO<sub>4</sub>, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65 °C, and washing in 0.1X SSC/0.1% SDS at 68 °C), and moderately  
5 stringent conditions (i.e., washing in 0.2X SSC/0.1% SDS at 42 °C). Other exemplary hybridization conditions are described herein in the examples.

In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37 °C (for 14-base oligonucleotides), 48 °C (for 17-base oligos), 55 °C  
10 (for 20-base oligonucleotides), and 60 °C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences.  
15 Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (*i.e.*, the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less). Such a sequence is said to have  
20 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, *e.g.*, mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by  
25 no more than 10% (90% sequence identity) and in a further variation of this embodiment, by no more than 5% (95% sequence identity). Substantially equivalent, *e.g.*, mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 90% sequence identity. Substantially equivalent nucleotide sequences of the invention can have lower  
30 percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65%

identity, more preferably at least about 75% identity, and most preferably at least about 95% identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence (*e.g.*, via a mutation which creates a spurious stop codon) should be disregarded. Sequence identity may be determined, *e.g.*, using the Jotun Hein method (Hein, J. (1990) *Methods Enzymol.* 183:626-645). Identity between sequences can also be determined by other methods known in the art, *e.g.* by varying hybridization conditions.

10       The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

      The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

      As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides that mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

      Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

### 3.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 1-113, 227-339, or 453-477; a polynucleotide  
5 encoding any one of the peptide sequences of SEQ ID NO: 114 – 226, 340 – 452 and 478-502; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polynucleotides of any one of SEQ ID NO: 1-113, 227-339, and 453-477. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the  
10 complement of any of the nucleotides sequences of SEQ ID NO: 1-113, 227-339, and 453-477; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide  
15 comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 114–226, 340–452 or 478-502. Domains of interest may depend on the nature of the encoded polypeptide; e.g., domains in receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains;  
20 domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, e.g., cDNA and genomic DNA, and RNA, e.g., mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a  
25 portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification  
30 and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For

example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO: 1-113, 227-339, and 453-477 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO: 1-113, 227-339, and 453-477 or a portion thereof as a  
5 probe. Alternatively, the polynucleotides of SEQ ID NO: 1-113, 227-339, and 453-477 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public  
10 databases, such as dbEST, gbpri, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited  
15 above. Polynucleotides according to the invention can have, *e.g.*, at least about 65%, at least about 70%, at least about 75%, at least about 80%, more typically at least about 90%, and even more typically at least about 95%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are  
20 nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO: 1-113, 227-339, and 453-477 or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most preferably greater than 17 nucleotides. Fragments of, *e.g.* 15, 17, or 20 nucleotides or more that are selective for  
25 (i.e. specifically hybridize to any one of the polynucleotides of the invention) are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

30 The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and

species variations can be routinely determined by comparing the sequences provided in SEQ ID NO: 1-113, 227-339, or 453-477, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NOs: 1-113, 227-339, or 453-477 with a sequence from another isolate of the same species. Furthermore, to  
5 accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present  
10 invention, including SEQ ID NOs: 1-113, 227-339, and 453-477, can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST, which stands for Basic Local Alignment Search Tool, is used to search for local sequence alignments (Altschul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy  
15 algorithm could also be used.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

20 The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences that  
25 encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably  
30 constructed by mutating the polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic acid alterations can be made at sites that differ in the

nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, *e.g.*, by substituting first with conservative choices (*e.g.*, hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (*e.g.*, hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

15 In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed

20 mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith, *Nucleic Acids Res.* 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of

25 template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid

30 and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., supra, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent  
5 degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression of these novel nucleic acids. Such DNA sequences include those that are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

10 Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA,  
15 amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the  
20 mature protein coding sequences corresponding to any one of SEQ ID NO: 1-113, 227-339, and 453-477, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

25 A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al. (1989) *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, e.g., plasmids, cosmids, lambda phage derivatives, phagemids, and  
30 the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide.

In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell.

Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be  
5 a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NOs: 1-113, 227-339, and 453-477 or a fragment thereof or any other polynucleotides of the invention. In one  
10 embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NOs: 1-113, 227-339, and 453-477 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences,  
15 including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBS, phagescript, PsiX174, pBluescript SK, pBS KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene);  
20 pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein  
25 recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the  
30 protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.



Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, *e.g.*, the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, *e.g.*, stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example,

pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

### 3.2.1 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1-113, 227-339, and 453-477, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID NO: 114 – 226, 340 – 452 or 478-502 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO: 1-113, 227-339, and 453-477 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding a nucleic acid disclosed herein (*e.g.*, SEQ ID NO:1-113, 227-339, and 453-477), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of a mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of a mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil,

beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v),  
5 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following  
10 subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The  
15 hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules  
20 can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered  
25 to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is  
30 an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual

$\beta$ -units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

5

### 3.2.2 RIBOZYMES AND PNA MOIETIES

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as a mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be designed based upon the nucleotide sequence of a DNA disclosed herein (*i.e.*, SEQ ID NO: 1-113, 227-339, and 453-477).  
10 For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a SECX-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Pat. No. 4,987,071; and Cech *et al.* U.S. Pat. No. 5,116,742. Alternatively, mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules.  
15 See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) *Anticancer Drug Des.* 6: 569-84; Helene. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14: 807-15.  
25

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see  
30 Hyrup *et al.* (1996) *Bioorg Med Chem* 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the

deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide  
5 synthesis protocols as described in Hyrup *et al.* (1996) above; Perry-O'Keefe *et al.* (1996) *PNAS* 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or  
10 inhibiting replication. PNAs of the invention can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.* (1996), above; Perry-O'Keefe (1996), above).

15 In another embodiment, PNAs of the invention can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA  
20 recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in  
25 Hyrup (1996) above and Finn *et al.* (1996) *Nucl Acids Res* 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.* (1989) *Nucl Acid Res* 17: 5973-88). PNA  
30 monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.* (1996) above). Alternatively,

chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. See, Petersen *et al.* (1975) *Bioorg Med Chem Lett* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre *et al.*, 1987, *Proc. Natl. Acad. Sci.* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, *e.g.*, Krol *et al.*, 1988, *BioTechniques* 6:958-976) or intercalating agents. (See, *e.g.*, Zon, 1988, *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

### 3.3 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell that drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, *ada*, *dhfr*, and the multifunctional CAD gene which

encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

5       The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE, dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host  
10       cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa  
15       cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can  
20       also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

25       Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts; described by Gluzman, *Cell* 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human  
30       epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of



primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking  
5 nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion  
10 chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

15 Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella*  
20 *typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

25 In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region  
30 with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be

comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences that affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences that alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, an enhancer that has broader or different cell-type specificity than the naturally occurring elements can replace a tissue-specific enhancer. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (*gpt*) gene.

The gene targeting or gene activation techniques, which can be used in accordance with this aspect of the invention, are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and

International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

### 3.4 POLYPEPTIDES OF THE INVENTION

5       The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO: 114 – 226, 340 – 452 or 478 – 502 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NOs: 1-113, 227-339, and 453-477 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides  
10   preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NOs: 1-113, 227-339, and 453-477 or (b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO: 114–226, 340–452 and 478–502 or (c)  
15   polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO: 114–226, 340–452 or 478–502 or the corresponding full length or mature protein; and “substantial equivalents” thereof (e.g., with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%,  
20   typically at least about 95%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity. Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO: 114–226, 340–452 and 478-502.

      Fragments of the proteins of the present invention that are capable of exhibiting  
25   biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., *Bio/Technology* 10, 773-778 (1992) and in R. S. McDowell, et al., *J. Amer. Chem. Soc.* 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such  
30   as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the disclosed nucleotide sequences. The mature form of such protein may be obtained by  
5 expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are  
10 fully secreted from the cell in which it is expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic  
15 acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments that differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

20 A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with  
25 proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic  
30 compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells that have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell that produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells that naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, e.g., Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag (1994); Sambrook, et al., in *Molecular Cloning: A Laboratory Manual*; Ausubel et al., *Current Protocols in Molecular Biology*. Polypeptide fragments that retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in *in vitro* binding assays that are well known in the art to identify molecules that bind to the polypeptides. These molecules

include but are not limited to, for e.g., small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell  
5 cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or  
10 other cell by the specificity of the binding molecule for SEQ ID NO: 114-226, 340-452 or 478-502.

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the  
15 protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications, in the peptide or DNA sequence, can be made by those skilled in the art using known techniques. Modifications  
20 of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art  
25 (see, e.g., U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting  
30 alanine-containing variant for biological activity. This type of analysis determines the

importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other immunological methodologies may also be easily made by those skilled in the art given  
5 the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for  
10 baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the MaxBat™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is  
15 "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange  
20 chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl™ or Cibacrom blue 3GA Sepharose™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity  
25 chromatography.

Alternatively, the protein of the invention may also be expressed in a form, which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His tag. Kits for expression and purification of such fusion proteins are  
30 commercially available from New England BioLabs (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an

epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, *e.g.*, silica gel having pendant methyl or other aliphatic groups can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, *e.g.*, targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, *e.g.*, antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes, dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties, which may be fused to the polypeptide, include therapeutic agents that are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

### 3.4.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs including, but are not limited to, the GCG program package,



including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Mol. Biol. 215:403-410 (1990), PSI-BLAST (Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMATRIX software (Wu et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), PFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference), SignalP software package (Nielsen H et al., Int. J. Neural Syst., Vol. 8, pp. 581 – 599 (1997), herein incorporated by reference) and the Kyte-Doolittle hydrophobicity prediction algorithm (J. Mol. Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

### 3.4.2 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide(s) according to the invention and the other polypeptide(s) are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus or in the middle.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (i.e., glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprise one or more domains fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, *e.g.*, cancer as well as modulating (*e.g.*, promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used to bind and to dimerize 2 receptors and thereby transduce an intracellular signal. The immunoglobulin fusion proteins may also be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available

that already encode a fusion moiety (e.g., a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

### 5           3.5 GENE THERAPY

Mutations in the polynucleotides of the invention gene may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states involving polypeptides of the invention. Delivery of a functional gene encoding  
10 polypeptides of the invention to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (e.g., adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (e.g., liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology  
15 see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured *ex*  
20 *vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense  
25 therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the  
30 present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered *in vivo* to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell, which drives expression of the polynucleotides in the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (e.g., by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (e.g., *ada*, *dhfr*, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences that affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for

enhancing or modifying transport or secretion properties of the protein, or other sequences that alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (*gpt*) gene.

The gene targeting or gene activation techniques that can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

### 3.6 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention *in vivo*, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi,

Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, e.g., homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

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### 3.7 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or

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vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including  
5 recombinant DNA molecules, cloned genes and degenerate variants thereof) or polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein  
10 expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or indirectly activate or inhibit the polypeptides of the invention (identified, e.g., via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular  
15 antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation or in one of the other physiological pathways described herein.

### 20 3.7.1 RESEARCH USES AND UTILITIES

The research community can use the polynucleotides provided by the present invention for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a  
25 particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR  
30 primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers

for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein  
5 (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The polypeptides provided by the present invention can similarly be used in  
10 assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at  
15 particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent  
20 grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology:  
25 Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

### 3.7.2 NUTRITIONAL USES

Polynucleotides and polypeptides of the present invention can also be used as  
30 nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source



of carbohydrate. In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

### 3.7.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of therapeutic compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK, HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology.

J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin- $\gamma$ , Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

- 5            Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al.,  
10    Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner,  
15    K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9--Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

- Assays for T-cell clone responses to antigens (which will identify, among others,  
20    proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter  
25    6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

### 3.7.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells *in vivo* or *ex vivo* is expected to maintain and expand cell populations in a totipotent or pluripotent state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, bone marrow inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium. Alternatively, stroma cells transfected with a polynucleotide that

encodes for the polypeptide of the invention can be used as a feeder layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

- 5           Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for generation of undifferentiated totipotent/pluripotent stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotent/pluripotent mRNA to
- 10          create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

- Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present
- 15          invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and
- 20          neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

- Expression of the polypeptide of the invention and its effect on stem cells can also
- 25          be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced
- 30          to differentiate into cardiomyocytes (Wobus et al., *Differentiation*, 48: 173-182, (1991); Klug et al., *J. Clin. Invest.*, 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L.

W. In: *Principles of Tissue Engineering eds.* Lanza et al., Academic Press (1997)).

Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

*In vitro* cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell sources (including hematopoietic stem cells and embryonic stem cells) and cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support e.g. as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

### 3.7.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/bone marrows (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various

stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

10        Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

15        Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992;

20        Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

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### 3.7.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

5 A polypeptide of the present invention that induces cartilage and/or bone growth in circumstances where bone is not normally formed has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also  
10 in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors  
15 of bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

20 Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a  
25 tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or  
30 ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention

may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be  
5 useful in the treatment of tendonitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central  
10 and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's,  
15 Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further, conditions that may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition  
20 of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or  
25 regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention  
30 may also exhibit angiogenic activity.



A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or  
5 inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);  
10 International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J.  
15 Invest. Dermatol 71:382-84 (1978).

### 3.7.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays  
20 are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune  
25 deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such  
30 as candidiasis. Of course, in this regard, proteins of the present invention may also be

useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders that may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, 5 Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (*e.g.*, anaphylaxis, 10 serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic 15 asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., 20 Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxicol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or 25 blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process that requires continuous exposure of the T cells to the suppressive agent. 30 Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and

persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without  
5 limitation B lymphocyte antigen functions (such as, for example, B7)), e.g., preventing  
high level lymphokine synthesis by activated T cells, will be useful in situations of tissue,  
skin and organ transplantation and in graft-versus-host disease (GVHD). For example,  
blockage of T cell function should result in reduced tissue destruction in tissue  
transplantation. Typically, in tissue transplants, rejection of the transplant is initiated  
10 through its recognition as foreign by T cells, followed by an immune reaction that  
destroys the transplant. The administration of a therapeutic composition of the invention  
may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an  
immunosuppressant. Moreover, a lack of costimulation may also be sufficient to  
anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term  
15 tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated  
administration of these blocking reagents. To achieve sufficient immunosuppression or  
tolerance in a subject, it may also be necessary to block the function of a combination of  
B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant  
20 rejection or GVHD can be assessed using animal models that are predictive of efficacy in  
humans. Examples of appropriate systems which can be used include allogeneic cardiac  
grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been  
used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as  
described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl.  
25 Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul  
ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used  
to determine the effect of therapeutic compositions of the invention on the development  
of that disease.

Blocking antigen function may also be therapeutically useful for treating  
30 autoimmune diseases. Many autoimmune disorders are the result of inappropriate  
activation of T cells that are reactive against self-tissue and which promote the

production of cytokines and autoantibodies involved in the pathology of the diseases.

Preventing the activation of auto-reactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of auto-reactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (e.g., a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T cells to induce a T cell mediated immune response against the transfected

tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and  $\beta_2$  microglobulin protein or an MHC class II alpha chain protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In

vitro antibody production, Mond, J. J. and Brunswick, M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnoli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

### 3.7.8 ACTIVIN/INHIBIN ACTIVITY

A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH); while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

### 3.7.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic

compositions (e.g. proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

5 A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

### 25 3.7.10 HEMOSTATIC AND THROMBOLYTIC ACTIVITY

A polypeptide of the invention may also be involved in hemostasis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving



or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

Therapeutic compositions of the invention can be used in the following:

- 5        Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

### 10            3.7.11 CANCER DIAGNOSIS AND THERAPY

- Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a
- 15       polynucleotide/polypeptide of the invention may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

- 20       Cancer treatments promote tumor regression by inhibiting tumor cell proliferation, inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced
- 25       tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma, acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers
- 30       including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers

including bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma, tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Karposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, e.g. reducing tumor size, slowing rate of tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without necessarily eradicating the cancer.

The composition can also be administered in therapeutically effective amounts as a portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D, Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine

sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (e.g. exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

*In vitro* models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These *in vitro* models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wiley-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30 (1974), mobility and invasive potential of tumor cells in Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available, e.g. from American Type Tissue Culture Collection catalogs.

### 3.7.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses. Receptors and ligands are also

useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

- 5           The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

          Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and  
10   Wiley- Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1- 7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

- 15           By way of example, the polypeptides of the invention may be used as a receptor for a ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

- Studies characterizing drugs or proteins as agonist or antagonist or partial agonists  
20   or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or toxin molecules by conventional methods. ("Guide to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of  
25   radioisotopes include, but are not limited to, tritium and carbon-14. Examples of colorimetric molecules include, but are not limited to, fluorescent molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

### 3.7.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques. The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (i.e., increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science* 282:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other

libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, *Curr. Opin. Biotechnol.* 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., *Mol. Biotechnol.*, 9(3):205-23 (1998); Hruby et al., *Curr Opin Chem Biol*, 1(1):114-19 (1997);  
5 Dorner et al., *Bioorg Med Chem*, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding  
10 assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The  
15 toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

#### 20 3.7.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide e.g. a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or  
25 dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (*i.e.*,  
30 increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous

ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population expresses the receptor of the invention whereas the other does not. The response of the two cell populations to the addition of ligands(s) is then compared. Alternatively, an expression  
5 library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides,  
10 oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host  
15 cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins involved in intracellular signaling can then be assayed for expected modifications i.e. phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

20

### 3.7.15 ANTI-INFLAMMATORY ACTIVITY

Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions  
25 (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without  
30 limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin

lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflammation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic myelogenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

#### 3.7.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not limited to acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

#### 3.7.17 NERVOUS SYSTEM DISORDERS

Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention



include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

- (i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions that sever a portion of the nervous system, or  
5 compression injuries;
- (ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;
- (iii) infectious lesions, in which a portion of the nervous system is destroyed or  
10 injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;
- (iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration  
15 associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;
- (v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency,  
20 Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;
- (vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;
- 25 (vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and
- (viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human immunodeficiency virus-associated myelopathy, transverse myelopathy  
30 or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

- (i) increased survival time of neurons in culture;
- (ii) increased sprouting of neurons in culture or *in vivo*;
- (iii) increased production of a neuron-associated molecule in culture or *in vivo*, *e.g.*, choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or
- (iv) decreased symptoms of neuron dysfunction *in vivo*.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, *etc.*, depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, *e.g.*, weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

### 3.7.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other  
5 parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting  
10 the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or  
15 other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or  
20 complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

### 3.7.19 IDENTIFICATION OF POLYMORPHISMS

25 The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis and treatment. Such polymorphisms may be associated with, e.g., differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and  
30 this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a

predisposition to inflammation or autoimmune disease makes possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA, which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately adjacent to the position of the polymorphism is extended with one or more labeled nucleotides). In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified nucleotide sequences of the present invention in order to detect the nucleotide sequences of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, e.g., by an antibody specific to the variant sequence.

### 3.7.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis are determined in an experimental animal model system. The experimental model system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et al., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but

rats may be injected at the base of the tail with an adjuvant mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of  
5 intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on  
10 the swelling of the joints as measured by a decrease of the arthritis score.

### 3.8 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides)  
15 of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

#### 3.8.1 EXAMPLE

20 One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An exemplary mode of administration is to deliver an intravenous bolus.  
25 The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about 0.01µg/kg to 100 mg/kg of body weight, with the preferred dose being about 0.1µg/kg to 10 mg/kg  
30 of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable

parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

### 3.9 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents that either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active

ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (e.g., at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers to that amount of the compound sufficient to result in amelioration of symptoms, *e.g.*, treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-

administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors; or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

### 3.9.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the



invention can be extrapolated from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

### 5           3.9.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations that can be used pharmaceutically. These  
10 pharmaceutical compositions may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered  
15 orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25  
20 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol,  
25 propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of  
30 the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of

a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may

be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations that can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection

suspensions may contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active  
5 ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the  
10 compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives,  
15 for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a co-solvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar  
20 surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without  
25 destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.* polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for  
30 dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of

delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent.

5 Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

10 The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such  
15 pharmaceutically acceptable base addition salts are those salts which retain the biological effectiveness and properties of the free acids and which are obtained by reaction with inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

20 The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B-lymphocytes will respond to antigen through their surface immunoglobulin receptor. T-lymphocytes will respond to antigen through  
25 the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies  
30 able to bind surface immunoglobulin and other molecules on B cells as well as antibodies

able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other  
5 pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the  
10 art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments that the  
15 patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be  
20 administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01  $\mu$ g to about 100 mg (preferably about 0.1  $\mu$ g to about 10 mg, more preferably about 0.1  $\mu$ g to about 1 mg) of protein or other active ingredient of the present  
25 invention per kg body weight. For compositions of the present invention that are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systemically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may  
30 desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing

and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention that may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above-mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being

cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly (ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly (vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which  
5 represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with  
10 other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary  
15 applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, *e.g.*,  
20 amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (*e.g.*, bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition  
25 of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also affect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such  
30 polynucleotides can be introduced either in vivo or ex vivo into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other



known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be  
5 introduced in vivo for therapeutic purposes.

### 3.9.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to  
10 achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in the method of the invention, the  
15 therapeutically effective dose can be estimated initially from appropriate *in vitro* assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the  $IC_{50}$  as determined in cell culture (*i.e.*,  
20 the concentration of the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and  
25 therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the  $LD_{50}$  (the dose lethal to 50% of the population) and the  $ED_{50}$  (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between  $LD_{50}$  and  $ED_{50}$ .  
30 Compounds that exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage

for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED<sub>50</sub> with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, *e.g.*, Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety that are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen that maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 µg/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 µg/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

#### 3.9.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device that may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions

comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

### 5           3.10 ANTIBODIES

Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, i.e., molecules that contain an antigen binding site that specifically binds (immunoreacts with) an  
10 antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain,  $F_{ab}$ ,  $F_{ab}'$  and  $F_{(ab)2}$  fragments, and an  $F_{ab}$  expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG<sub>1</sub>, IgG<sub>2</sub>, and  
15 others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen  
20 to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein, such as an  
25 amino acid sequence shown in SEQ ID NO: 114-226, 340-452, 478-502, and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino  
30 acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of -related protein that is located on the surface of the protein, *e.g.*, a hydrophilic region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

### 3.10.1 POLYCLONAL ANTIBODIES

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the

mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and *Corynebacterium parvum*, or similar immunostimulatory agents. Additional examples of adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

### 3.10.2 MONOCLONAL ANTIBODIES

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an

immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as

radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

### 3.10.3 HUMANIZED ANTIBODIES

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')<sub>2</sub> or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)).

### 3.10.4 HUMAN ANTIBODIES

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 *Immunol Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal



antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human  
5 B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)). Similarly, human antibodies can be  
10 made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos.  
15 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (Bio/Technology 10, 779-783 (1992)); Lonberg et al. (Nature 368 856-859 (1994)); Morrison (Nature 368, 812-13 (1994)); Fishwild et al. (Nature Biotechnology 14, 845-51 (1996)); Neuberger (Nature Biotechnology 14, 826 (1996)); and Lonberg and Huszar (Intern. Rev. Immunol. 13 65-93 (1995)).

20 Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci  
25 encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The  
30 preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse<sup>TM</sup> as disclosed in PCT publications WO 96/33735 and WO 96/34096. This

animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

### 3.10.5 F<sub>ab</sub> FRAGMENTS AND SINGLE CHAIN ANTIBODIES

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see e.g., U.S.

Patent No. 4,946,778). In addition, methods can be adapted for the construction of  $F_{ab}$  expression libraries (see e.g., Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal  $F_{ab}$  fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an  $F_{(ab)_2}$  fragment produced by pepsin digestion of an antibody molecule; (ii) an  $F_{ab}$  fragment generated by reducing the disulfide bridges of an  $F_{(ab)_2}$  fragment; (iii) an  $F_{ab}$  fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv)  $F_v$  fragments.

### 3.10.6 BISPECIFIC ANTIBODIES

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, *Nature*, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain

binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')<sub>2</sub> bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')<sub>2</sub> fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med.

175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')<sub>2</sub> molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and  
5 normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol.  
10 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc.  
15 Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V<sub>H</sub>) connected to a light-chain variable domain (V<sub>L</sub>) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V<sub>H</sub> and V<sub>L</sub> domains of one fragment are forced to pair with the complementary V<sub>L</sub> and V<sub>H</sub>  
20 domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., J. Immunol. 147:60 (1991).  
25 Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (Fc<sub>γ</sub> R), such as Fc<sub>γ</sub> RI(CD64), Fc<sub>γ</sub> RII(CD32) and  
30 Fc<sub>γ</sub> RIII(CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to

cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

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### 3.10.7 HETEROCONJUGATE ANTIBODIES

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

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### 3.10.8 EFFECTOR FUNCTION ENGINEERING

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

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### 3.10.9 IMMUNOCONJUGATES

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the

circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is in turn conjugated to a cytotoxic agent.

### 3.11 COMPUTER READABLE SEQUENCES

5 In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium that can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as  
10 CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a  
15 process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a  
20 computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented  
25 in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (e.g. text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide  
30 sequence information of the present invention.



By providing any of the nucleotide sequences SEQ ID NOs: 1-113, 227-339, or 453-477, or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NOs: 1-113, 227-339, or 453-477 in computer readable form, a skilled artisan can routinely access the sequence  
5 information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to  
10 identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein-encoding fragments and may be useful in producing commercially important proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means,  
15 software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for  
20 use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present  
25 invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs that are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means.  
30 Search means are used to identify fragments or regions of a known sequence that match a particular target sequence or target motif. A variety of known algorithms are disclosed

publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software include, but are not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize  
5 that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will  
10 be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

15 As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration that is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid  
20 target motifs include, but are not limited to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

### 3.12 TRIPLE HELIX FORMATION

In addition, the fragments of the present invention, as broadly described, can be  
25 used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix-see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al.,  
30 Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense-Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as

Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information  
5 contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

### 3.13 DIAGNOSTIC ASSAYS AND KITS

The present invention further provides methods to identify the presence or  
10 expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the  
15 polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed polynucleotides, so that if a  
20 polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polypeptide of the invention is detected in the sample.

25 In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection  
30 methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available

hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard, T., *An Introduction to Radioimmunoassay and Related Techniques*, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., *Techniques in Immunocytochemistry*, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., *Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology*, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container, which will accept the test sample, a container, which contains the antibodies used in the assay, containers, which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers, which contain the reagents used to detect the bound antibody or probe. Types of detection reagents include labeled nucleic acid

probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats that are well known in the art.

### 3.14 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (e.g., where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, e.g., Kunkel et al., U.S. Pat. No. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

### 3.15 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide set forth in SEQ ID NO: 114 – 226, 340 – 452 and 478 – 502 encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NOs: 1-113, 227-339, and 453-477, or which binds to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

- (a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and
- (b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds that modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds identified via such methods can include compounds that modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to

a specific peptide sequence, in order to generate rationally designed antipeptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

5 In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the  
10 expression of either a single ORF or multiple ORFs that rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester, ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives that have base attachment  
15 capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix-see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense-  
20 Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences  
25 of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents that bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents that bind to a protein encoded by one of the ORFs of the present invention can be formulated using known techniques to generate a  
30 pharmaceutical composition.

### 3.16 USE OF NUCLEIC ACIDS AS PROBES

Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived  
5 from any of the nucleotide sequences SEQ ID NOs: 1-113, 227-339, and 453-477. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from any of the nucleotide sequences SEQ ID NOs: 1-113, 227-339, and 453-477 can be used as an indicator of the presence of RNA of cell type of such a tissue in a sample. Preferably a hybridization probe from any of nucleotide  
10 sequences SEQ ID NO: 1-113, 227-339, and 453-477 can be used as an indicator of bone marrow tissue.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such  
15 probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The probe will comprise a discrete nucleotide sequence for the detection of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include  
20 the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for  
25 mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well-known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known  
30 chromosomes, and the like. The technique of fluorescent in situ hybridization of



chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent *in situ* hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data.

- 5 Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences  
10 between normal, carrier or affected individuals.

### 3.17 PREPARATION OF SEQUENCING CHIPS AND ARRAYS

A basic example is using 6-mers attached to 50 micron surfaces to give a chip with dimensions of 3 x 3 mm which can be combined to give an array of 20 x 20 cm.

- 15 Another example is using 9-mer oligonucleotides attached to 10 x 10 microns surface to create a 9-mer chip, with dimensions of 5 x 5 mm. 4000 units of such chips may be used to create a 30 x 30 array. In an array in which 4,000 to 16,000 oligochips are arranged into a square array. A plate, or collection of tubes, as also depicted, may be packaged with the array as part of the sequencing kit.

- 20 The arrays may be separated physically from each other or by hydrophobic surfaces. One possible way to utilize the hydrophobic strip separation is to use technology such as the Iso-Grid Microbiology System produced by QA Laboratories, Toronto, Canada.

- Hydrophobic grid membrane filters (HGMF) have been in use in analytical food  
25 microbiology for about a decade where they exhibit unique attractions of extended numerical range and automated counting of colonies. One commercially available grid is ISO-GRID™ from QA Laboratories Ltd. (Toronto, Canada) which consists of a square (60 x 60 cm) of polysulfone polymer (Gelman Tuffryn HT-450, .45 um pore size) on which is printed a black hydrophobic ink grid consisting of 1600 (40 x 40) square cells.  
30 HGMF have previously been inoculated with bacterial suspensions by vacuum filtration and incubated on the differential or selective media of choice.

Because the microbial growth is confined to grid cells of known position and size on the membrane, the HGMF functions more like an MPN apparatus than a conventional plate or membrane filter. Peterkin et al. (1987) reported that these HGMFs can be used to propagate and store genomic libraries when used with a HGMF replicator. One such instrument replicates growth from each of the 1600 cells of the ISO-GRID and enables many copies of the master HGMF to be made (Peterkin et al., 1987).

Sharpe et al. (1989) also used ISO-GRID HGMF from QA Laboratories and an automated HGMF counter (MI-100 Interpreter) and RP-100 Replicator. They reported a technique for maintaining and screening many microbial cultures.

Peterkin and colleagues later described a method for screening DNA probes using the hydrophobic grid-membrane filter (Peterkin et al., 1989). These authors reported methods for effective colony hybridization directly on HGMFs. Previously, poor results had been obtained due to the low DNA binding capacity of the epoxysulfone polymer on which the HGMFs are printed. However, Peterkin et al. (1989) reported that the binding of the DNA to the surface of the membrane was improved by treating the replicated and incubated HGMF with polyethyleneimine, a polycation, prior to contact with DNA. Although this early work uses cellular DNA attachment, and has a different objective to the present invention, the methodology described may be readily adapted for Format 3 SBH.

In order to identify useful sequences rapidly, Peterkin et al. (1989) used radiolabeled plasmid DNA from various clones and tested its specificity against the DNA on the prepared HGMFs. In this way, DNA from recombinant plasmids was rapidly screened by colony hybridization against 100 organisms on HGMF replicates that can be easily and reproducibly prepared.

Manipulation with small (2-3 mm) chips, and parallel execution of thousands of the reactions. The solution of the invention is to keep the chips and the probes in the corresponding arrays. In one example, chips containing 250,000 9-mers are synthesized on a silicon wafer in the form of 8 x 8 mM plates (15 uM/oligonucleotide, Pease et al., 1994) arrayed in 8 x 12 format (96 chips) with a 1 mM groove in between. Probes are added either by multichannel pipette or pin array, one probe on one chip. To score all

4000 6-mers, 42 chip arrays have to be used, either using different ones, or by reusing one set of chip arrays several times.

In the above case, using the earlier nomenclature of the application,  $F=9$ ;  $P=6$ ; and  $F+P=15$ . Chips may have probes of formula  $B_xN_n$ , where  $x$  is a number of specified bases  $B$ ; and  $n$  is a number of non-specified bases, so that  $x=4$  to  $10$  and  $n=1$  to  $4$ . To achieve more efficient hybridization, and to avoid potential influence of any support oligonucleotides, the specified bases can be surrounded by unspecified bases, thus represented by a formula such as  $(N)_nB_x(N)_m$ .

### 3.18 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, i.e., small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers. Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata *et al.*, 1985; Dahlen *et al.*, 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller *et al.*, 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, e.g., Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used. Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed CovaLink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups ( $>NH$ ) that serve as bridge-heads for further covalent

coupling. CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.*, (1991) Anal. Biochem. 198(1) 138-42).

5           The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen *et al.*, (1991). In this technology, a phosphoramidate bond is employed (Chu *et al.*, (1983) Nucleic Acids Res. 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end  
10 of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via a phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

          More specifically, the linkage method includes dissolving DNA in water (7.5 ng/ul)  
15 and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M 1-methylimidazole, pH 7.0 (1-MeIm<sub>7</sub>), is then added to a final concentration of 10 mM 1-MeIm<sub>7</sub>. A ss DNA solution is then dispensed into CovaLink NH strips (75 ul/well) standing on ice.

          Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC),  
20 dissolved in 10 mM 1-MeIm<sub>7</sub>, is made fresh and 25 ul added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, e.g., Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

25           It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The  
30 oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not

cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) *Science* 251(4995) 767-73, incorporated herein by reference. Probes may also be immobilized on nylon supports as described by Van Ness *et al.* (1991) *Nucleic Acids Res.* 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) *Anal. Biochem.* 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) *Proc. Natl. Acad. Sci. USA* 91(11) 5022-6, incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

### 3.19 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification

methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The results of these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, CviJI, described by Fitzgerald *et al.* (1992) Nucleic Acids Res. 20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease CviJI normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme (CviJI\*\*), yield a quasi-random distribution of DNA fragments from the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a CviJI\*\* digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that CviJI\*\* restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 ug instead of 2-5 ug); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed).

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for

hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

### 5           3.20    PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher  
10   than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm<sup>2</sup>, depending on the type of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the subarrays may represent replica  
15   spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate (all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane. Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are  
20   identical, the dot span may be 1 mm<sup>2</sup> and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers e.g. a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic strips. A fixed physical spacer is not preferred for imaging by  
25   exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader aspects of the present invention not be limited to the disclosure of  
30   the following examples. The present invention is not to be limited in scope by the exemplified embodiments that are intended as illustrations of single aspects of the invention,

and compositions and methods that are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon consideration of the present preferred embodiments. Consequently, the only limitations that should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

#### 4.0 EXAMPLES

##### 4.1 EXAMPLE 1

##### 10 Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosomes using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for the vector sequences that flank the inserts. Clones from cDNA libraries were spotted on nylon membrane filters and screened with oligonucleotide probes (e.g., 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones from each cluster were selected for sequencing.

The sequence of the amplified inserts, in some cases, was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences.

##### 4.2 EXAMPLE 2

##### Novel Nucleic Acids

25 The novel nucleic acids of the present invention were assembled from sequences that were obtained from a cDNA library by methods described in Example 1 above, and in some cases sequences obtained from one or more public databases. The nucleic acids of SEQ ID NO: 1-113, inclusive, were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend some of the seed ESTs into an extended assemblage,



by pulling additional sequences from different databases (i.e., Hyseq's database containing EST sequences, dbEST version 119, gb pri 119, and UniGene version 119, Geneseq October version, and Genscan, Genemark and Hyseq gene predictions on human genomic sequence from the human genome project updated October 2000) that belong to this  
 5 assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

### 10 4.3 EXAMPLE 3

#### Further Characterization

Clusters from Example 1 were identified which were expressed in bone marrow tissue cDNA libraries, but not in other tissues. Novel nucleic acids were assembled by the method of Example 2. A subset of the assembled nucleic acids comprising sequences from  
 15 the identified clusters was selected. This subset includes SEQ ID NO: 1-113. The tissue sources in which SEQ ID NO: 1-113 were exclusively expressed were found to be in BMD001 and BMD002 bone marrow libraries (Clontech).

The homologies for SEQ ID NO:1-113, and the corresponding peptide sequences, SEQ ID NO: 114-226, were obtained by performing various searches as shown in Tables  
 20 1A to 1D and as discussed herein.

The homologous sequences to the amino acid sequences corresponding to SEQ ID NO: 1-113 were obtained by a BLASTP version 2.0a1 19MP-WashU search against the Geneseq database updated November 9, 2000, update 23 for year 2000 (Derwent), using the BLAST algorithm. The homologues for the amino acid sequences corresponding to  
 25 SEQ ID NO: 1-113 from Geneseq are shown in Table 1A below.

**TABLE 1A**

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
2	Y51328	196(74.1bits)	2.9e-15	41	Y51328 Human KLIMP protein. Length = 1103
3	Y27621	489(177.2bits)	1.0e-46	71	Y27621 Human secreted protein

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					encoded by gene No. 55. Length = 193
8	Y05375	676(243.0bits)	1.6e-66	41	Y05375 Human HCMV inducible gene protein, SEQ ID NO 18. Length = 490
9	W62625	1526(542.2bits)	1.4e-156	87	W62625 Mus musculus SOCS14 protein. Length = 542
10	W81172	612(220.5bits)	2.6e-246	84	W81172 Human BAZ1-beta protein #1. Length = 1527
11	P91655	143(55.4bits)	1.0e-06	37	P91655 Eimeria cell surface antigen. Length = 259
13	G41284	240(89.5bits)	2.5e-20	32	G41284 Arabidopsis thaliana protein fragment SEQ ID NO: 51346. Length = 284
14	Y79380	131(51.2bits)	1.3e-08	30	Y79380 Human ATP binding cassette ABCA1 (ABC1) protein. Length = 2201
15	Y96965	933(333.5bits)	3.7e-125	100	Y96965 Human nuclear dual-specificity phosphatase. Length = 893
16	G14400	393(143.4bits)	1.6e-36	35	G14400 Arabidopsis thaliana protein fragment SEQ ID NO: 14248. Length = 414
17	G43692	469(170.2bits)	1.8e-45	28	G43692 Arabidopsis thaliana protein fragment SEQ ID NO: 54640. Length = 776
18	G48638	342(125.4bits)	1.3e-29	38	G48638 Arabidopsis thaliana protein fragment SEQ ID NO: 61443. Length = 1544

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
24	Y73384	135(52.6bits)	1.1e-08	75	Y73384 HTRM clone 2284580 protein sequence. Length = 293
25	Y39779	194(73.4bits)	5.7e-14	35	Y39779 CBMACD04 protein sequence. Length = 353
26	G31980	388(141.6bits)	5.3e-36	40	G31980 Arabidopsis thaliana protein fragment SEQ ID NO: 38498. Length = 476
27	Y70440	332(121.9bits)	2.8e-32	48	Y70440 Human Notch signalling protein, Deltex (hZDX)-4. Length = 405
28	Y01072	347(127.2bits)	1.2e-30	32	Y01072 Rat I(3)mbt protein sequence. Length = 826
29	Y01072	347(127.2bits)	1.2e-30	32	Y01072 Rat I(3)mbt protein sequence. Length = 826
31	Y27748	784(281.0bits)	3.0e-77	81	Y27748 Human secreted protein encoded by gene No. 37. Length = 296
32	G02097	337(123.7bits)	1.3e-30	82	G02097 Human secreted protein, SEQ ID NO: 6178. Length = 90
34	W89026	1958(694.3bits)	2.3e-202	99	W89026 Polypeptide fragment encoded by gene 165. Length = 424
35	Y70247	352(129.0bits)	3.4e-32	97	Y70247 C-terminal region of human Polycystin-L protein. Length = 125
42	Y92241	2297(813.6bits)	2.7e-238	100	Y92241 Human cancer associated antigen precursor (MO-REN-46). Length = 914
44	Y66750	1356(482.4bits)	1.4e-138	99	Y66750 Membrane-bound protein PRO1287. Length = 532

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
45	Y79183	163(62.4bits)	4.5e-11	41	Y79183 Haematopoietic stem cell specific protein. Length = 631
48	Y84544	155(59.6bits)	1.8e-06	31	Y84544 A human collagen 1 (alpha1) protein helical region. Length = 1057
49	R47201	391(142.7bits)	8.6e-58	27	R47201 DPM2 mannosyl transferase. Length = 817
50	Y60434	664(238.8bits)	3.0e-65	100	Y60434 Human normal bladder tissue EST encoded protein 106. Length = 206
52	W99716	772(276.8bits)	1.1e-76	86	W99716 Human lysophosphatidic acid acyltransferase. Length = 334
53	W17523	268(99.4bits)	5.9e-22	35	W17523 Human beta-B2-crystallin. Length = 205
57	Y05768	695(249.7bits)	1.6e-68	95	Y05768 Human PRO216 (vitellogenic carboxypeptidase homologue). Length = 452
60	Y86211	995(355.3bits)	2.5e-100	100	Y86211 Nuclear transport protein clone hfb066 protein sequence. Length = 367
62	R32705	113(44.8bits)	3.1e-06	31	R32705 SSP-534 polypeptide. Length = 107
65	Y01160	341(125.1bits)	5.0e-31	100	Y01160 Polypeptide fragment encoded by gene 1. Length = 166
67	Y92902	171(65.3bits)	4.0e-16	33	Y92902 Human cerebral organic anion transporter OAT3 protein. Length = 542
70	Y81609	235(87.8bits)	1.4e-15	26	Y81609 Streptococcus

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					pneumoniae type 4 protein sequence #109. Length = 1237
71	Y83091	1289(458.8bits)	1.8e-131	100	Y83091 F-box protein FBP-23. Length = 621
72	W64518	270(100.1bits)	5.4e-29	24	W64518 Adenylate cyclase protein. Length = 1874
74	Y82708	2046(725.3bits)	1.1e-211	57	Y82708 Human apoptosis related protein ABP130 SEQ ID NO:6. Length = 1220
75	Y74093	244(91.0bits)	9.6e-21	96	Y74093 Human prostate tumor EST fragment derived protein #280. Length = 70
82	G03267	172(65.6bits)	4.1e-13	59	G03267 Human secreted protein, SEQ ID NO: 7348. Length = 111
84	Y99666	1631(579.2bits)	1.0e-167	100	Y99666 Human GTPase associated protein-17. Length = 698
88	R31348	128(50.1bits)	3.9e-07	46	R31348 Jaagsiekte retrovirus Pol protein. Length = 870
94	Y92942	772(276.8bits)	1.1e-76	69	Y92942 Rat MAGUIN 1 protein. Length = 1032
95	Y43523	163(62.4bits)	5.6e-11	28	Y43523 Human CCCTC-binding factor (CTCF) protein. Length = 727
96	W99716	1015(362.4bits)	1.9e-102	100	W99716 Human lysophosphatidic acid acyltransferase. Length = 334
97	Y24054	2962(1047.7bits)	9.2e-309	99	Y24054 A human beta-transducin repeat containing protein. Length = 569

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
99	G01698	330(121.2bits)	7.4e-30	98	G01698 Human secreted protein, SEQ ID NO: 5779. Length = 66
100	W40073	703(252.5bits)	2.2e-69	100	W40073 Human eosinophil-derived basic protein EBPH. Length = 225
110	Y53678	367(134.2bits)	1.4e-38	31	Y53678 Sequence gi/4426611/gb/AAD204501 from an alignment with protein 274.
111	P94260	134(52.2bits)	3.8e-07	24	P94260 41kD protein of T. colubriformis. Length = 235
112	P91071	210(79.0bits)	6.5e-16	32	P91071 N-alpha-acetyl transferase. Length = 847
113	W63043	129(50.5bits)	2.4e-06	28	W63043 Streptococcus uberis bovine lactoferrin binding protein. Length = 561

The homologous sequences to the amino acid sequences corresponding to SEQ ID NO: 1-113 were also obtained by a BLASTP version 2.0al 19MP-WashU search against the NCBI Genbank nr database updated November 10, 2000, using the BLAST algorithm. The homologues for the amino acid sequences corresponding to SEQ ID NO: 1-113 from Genbank are shown in Table 1B below.

TABLE 1B

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
1	BAB15741.1	810(290.2bits)	1.6e-79	78	(AK024451) FLJ00043 protein [Homo sapiens] Length = 1415
2	YB3D_SCHPO	275(101.9bits)	1.3e-22	54	YB3D_SCHPO PUTATIVE KINESIN-LIKE PROTEIN C2F12.13 >pir

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
3	NP_060512.1	414(150.8bits)	4.5e-74	34	hypothetical protein FLJ10260 [Homo sapiens] >dbj BAA91512.1  (AK001122) unnamed protein product [Homo sapiens]
4	NP_060512.1	333(122.3bits)	2.3e-29	44	hypothetical protein FLJ10260 [Homo sapiens] >dbj BAA91512.1  (AK001122) unnamed protein product [Homo sapiens]
6	NP_006708.1	533(192.7bits)	3.8e-51	68	spindlin [Homo sapiens] >gb AAD43035.1  (AF106682) spindlin [Homo sapiens]
7	T16443	225(84.3bits)	8.9e-18	45	T16443 hypothetical protein F53B1.2- Caenorhabditis elegans >gb
8	NP_001539.1	1192(424.7bits)	5.7e-121	66	interferon-induced protein with tetratricopeptide repeats 1; Interferon, alpha-inducible protein (MW 56kD);
9	NP_054730.1	963(344.1bits)	1.0e-96	59	KIAA0671 gene product [Homo sapiens] >dbj BAA31646.1  (AB014571) KIAA0671 protein [Homo sapiens]
10	AAD04720.1	2682(949.2bits)	1.4e-282	99	(AC005074) similar to U47321 (PID:g1245146) [Homo sapiens] Length = 972
11	NP_006039.1	6711(2367.4bits)	0.0	100	ubiquitination factor E4B (homologous to yeast UFD2); clone 686 protein [Homo sapiens] >gb AAD02233.1  (AF043117)
13	CAC07197.1	1008(359.9bits)	1.8e-101	95	(AL035456) dJ1099D15.1 (A putative DNAJ protein) [Homo sapiens]

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
14	NP_005493.1	131(51.2bits)	2.2e-08	30	ATP-binding cassette, sub-family A member 1; ATP-binding cassette 1; high density lipoprotein deficiency,
15	CAB63063.1	530(191.6bits)	2.3e-60	53	(AL096767) dJ579N16.2 (SET binding factor 1) [Homo sapiens] Length = 1631
16	BAB01687.1	2016(714.7bits)	2.7e-208	96	(AB046105) unnamed protein product [Macaca fascicularis] Length = 419
17	NP_060759.1	1892(671.1bits)	3.8e-195	99	hypothetical protein FLJ10979 [Homo sapiens] >dbj BAA91935.1  (AK001841) unnamed protein product [Homo sapiens]
18	BAB15495.1	1044(372.6bits)	2.7e-105	98	(AK026518) unnamed protein product [Homo sapiens] Length = 317
19	BAA91960.1	1206(429.6bits)	1.9e-122	100	(AK001885) unnamed protein product [Homo sapiens] Length = 235
20	BAB15707.1	324(119.1bits)	5.4e-29	80	(AK027251) unnamed protein product [Homo sapiens] Length = 325
25	AAA36767.1	1006(359.2bits)	2.9e-101	94	(L32162) transcription factor [Homo sapiens] Length = 450
26	NP_064654.1	900(321.9bits)	5.0e-90	81	cAMP inducible 2 protein [Mus musculus] >gb AAD24571.1 AF121081_1 (AF121081) cAMP inducible 2 protein [Mus
27	AAF65193.1	322(118.4bits)	4.4e-28	46	AF184236_1 (AF184236) deltex 2 [Gallus gallus] Length = 403
28	NP_057413.1	1604(569.7bits)	1.2e-164	99	RU1 [Homo sapiens] >gb AAF19794.1 AF168132_1 (AF168132) RU1 [Homo sapiens]
29	NP_057413.1	1604(569.7bits)	1.2e-164	99	RU1 [Homo sapiens] >gb AAF19794.1 AF168132_1 (AF168132) RU1 [Homo sapiens]



SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
31	NP_036247.1	6370(2247.4bits)	0.0	100	CASP8 associated protein 2; FLICE associated huge [Homo sapiens] >gb AAF03367.1  (AF154415) FLASH [Homo sapiens]
32	AAF58683.1	436(158.5bits)	1.9e-40	66	(AE003826) CG9062 gene product [Drosophila melanogaster] Length = 680
34	BAA34516.1	4924(1738.4bits)	0.0	100	(AB018339) KIAA0796 protein [Homo sapiens] Length = 1080
35	AAD08695.1	352(129.0bits)	4.1e-31	97	(AF094827) PKD2L [Homo sapiens] Length = 710
36	BAA97672.1	2823(998.8bits)	8.3e-294	92	(AB031230) protein containing CXXC domain 2 [Homo sapiens] Length = 827
39	BAB14213.1	1166(415.5bits)	3.2e-118	100	(AK022734) unnamed protein product [Homo sapiens] Length = 685
42	BAA25475.1	2297(813.6bits)	4.5e-238	100	(AB011121) KIAA0549 protein [Homo sapiens] Length = 469
43	AAB63375.1	135(52.6bits)	2.2e-08	44	(AF003352) unknown [Mus musculus] Length = 309
44	NP_060841.1	1495(531.3bits)	4.4e-153	100	hypothetical protein FLJ11264 [Homo sapiens] >dbj BAA92093.1  (AK002126) unnamed protein product [Homo sapiens]
45	BAB13443.1	390(142.3bits)	6.2e-35	95	(AB046837) KIAA1617 protein [Homo sapiens] Length = 904
48	BAA20781.1	3859(1363.5bits)	0.0	100	(AB002321) KIAA0323 [Homo sapiens] Length = 724
49	NP_009102.1	3982(1406.8bits)	0.0	100	protein-O-mannosyltransferase 1 [Homo sapiens] >gb AAD41246.1  (AF095150) protein O-mannosyl-transferase 1 [Homo

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
50	T12488	994(355.0bits)	5.4e-100	92	T12488 hypothetical protein DKFZp569D2231.1-human (fragment) >emb
51	NP_064505.1	3528(1247.0bits)	0.0	99	UDP-glucose:glycoprotein glucosyltransferase 1 [Homo sapiens] >gb AAF66232.1 AF227905_1 (AF227905)
52	NP_061213.1	668(240.2bits)	1.9e-65	87	putative lysophosphatidic acid acyltransferase [Mus musculus] >gb AAB66338.1  (AF015811) putative lysophosphatidic
53	AAB53791.1	5700(2011.6bits)	0.0	100	(U83115) non-lens beta gamma-crystallin like protein [Homo sapiens]
57	NP_067639.1	695(249.7bits)	2.6e-68	95	serine carboxypeptidase 1 precursor protein [Homo sapiens] >gb AAG16692.1 AF282618_1 (AF282618) serine
59	BAB14682.1	617(222.3bits)	4.8e-60	91	(AK023794) unnamed protein product [Homo sapiens] Length = 261
60	NP_060672.1	1284(457.0bits)	1.0e-130	100	hypothetical protein FLJ10747 [Homo sapiens] >dbj BAA91786.1  (AK001609) unnamed protein product [Homo sapiens]
61	AAF53976.1	423(154.0bits)	1.7e-39	45	(AE003669) CG9241 gene product [Drosophila melanogaster] Length = 581
62	NP_055494.1	413(150.4bits)	2.0e-38	43	KIAA0092 gene product [Homo sapiens] >dbj BAA07654.1  (D42054) KIAA0092 gene product is distantly
63	BAA86582.1	187(70.9bits)	4.1e-13	66	(AB033094) KIAA1268 protein [Homo sapiens]

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					Length = 1023
65	NP_033590.1	192(72.6bits)	1.8e-12	29	zinc finger protein 64 [Mus musculus] >gb AAC53039.1  (U49046) Zfp64 [Mus musculus]
67	AAB67044.1	999(356.7bits)	1.6e-100	94	(AC002464) organic cation transporter; 50% similarity to JC4884 (PID:g2143892) [Homo sapiens]
68	BAA76766.1	1194(425.4bits)	3.5e-121	95	(AB023139) KIAA0922 protein [Homo sapiens] Length = 790
69	NP_006599.1	1720(610.5bits)	6.3e-177	99	putative homeodomain transcription factor; putative homeodomain transcription factor 1 [Homo sapiens]
70	BAA86445.1	4556(1608.9bits)	0.0	100	(AB032957) KIAA1131 protein [Homo sapiens] Length = 1620
71	CAB37981.1	1289(458.8bits)	3.0e-131	100	(AL022395) dJ273N12.1 (PUTATIVE protein based on EST matches)-[Homo sapiens] >gb
72	NP_067689.1	3588(1268.1bits)	0.0	92	Circadian Oscillatory Protein (SCOP) [Rattus norvegicus] >dbj BAA77767.1  (AB023624) SCOP [Rattus norvegicus]
74	AAF78243.1	3568(1261.1bits)	0.0	100	AF274863_1 (AF274863) secretory pathway component Sec31B-1 [Homo sapiens]
75	NP_057696.1	303(111.7bits)	9.1e-27	96	HT015 protein; hypothetical protein PRO1278 [Homo sapiens] >gb AAF64141.1 AF2 23466_1 (AF223466) HT015 protein [Homo

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
81	BAA86464.1	577(208.2bits)	8.4e-56	100	(AB032976) KIAA1150 protein [Homo sapiens] Length = 499
82	10879345 ref	162(62.1bits)	2.3e-14	63	hypothetical protein XP_000918.1 [Homo sapiens]
83	AAF69643.1	347(127.2bits)	2.0e-31	100	AF119917_51 (AF119889) PRO2667 [Homo sapiens] Length = 186
84	BAA83043.1	4723(1667.6bits)	0.0	100	(AB029014) KIAA1091 protein [Homo sapiens] Length = 1359
87	AAC52011.1	156(60.0bits)	1.4e-10	69	(U49974) mariner transposase [Homo sapiens] Length = 351
88	CAA76879.1	149(57.5bits)	3.8e-09	45	(Y17832) pol protein [Human endogenous retrovirus K] Length = 872
94	T18293	772(276.8bits)	1.8e-76	69	T18293 guanylate kinase-interacting protein 1 Maguin-1, membrane- associated-rat >gb
95	T12509	346(126.9bits)	2.5e-31	98	T12509 hypothetical protein DKFZp434F162.1- human (fragment) >emb
96	NP_061213.1	785(281.4bits)	7.6e-78	99	putative lysophosphatidic acid acyltransferase [Mus musculus] >gb AAB66338.1  (AF015811) putative lysophosphatidic
97	AAD08702.1	3158(1116.7bits)	0.0	100	(AF101784) b-TRCP variant E3RS-IkappaB [Homo sapiens] Length = 605
99	NP_008942.1	1089(388.4bits)	4.6e-110	94	NP_008942.1
100	NP_006084.1	703(252.5bits)	3.7e-69	100	proteoglycan 3; prepro-major basic protein homolog [Homo sapiens] >gb AAD24471.1 AF1 32209_1 (AF132209) prepro-major

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
102	BAB15721.1	1729(613.7bits)	7.0e-178	97	(AK024431) FLJ00020 protein [Homo sapiens] Length = 1142
104	BAA34485.1	213(80.0bits)	2.9e-16	30	(AB018308) KIAA0765 protein [Homo sapiens] Length = 594
105	CAB70896.1	822(294.4bits)	9.1e-82	100	(AL137727) hypothetical protein [Homo sapiens] Length = 174
106	BAA34221.1	201(75.8bits)	9.5e-16	63	(AB013454) NaPi-2 beta [Rattus norvegicus] Length = 327
110	BAA92545.1	4348(1535.6bits)	0.0	98	(AB037728) KIAA1307 protein [Homo sapiens] Length = 1678
111	BAB13459.1	478(173.3bits)	7.1e-44	84	(AB046853) KIAA1633 protein [Homo sapiens] Length = 1561
112	BAB14562.1	758(271.9bits)	5.5e-75	85	(AK023402) unnamed protein product [Homo sapiens] Length = 526
113	NP_034009.1	834(298.6bits)	4.9e-83	90	carnitine deficiency- associated gene expressed in ventricle 1 [Mus musculus] >sp O35594 CDV1_M OUSE CARNITINE

- The homologous sequences to SEQ ID NO: 1-113 were also obtained by a BLASTN version 2.0a1 19MP-WashU search against the Geneseq database updated November 9, 2000, update 23 for year 2000 (Derwent), using the BLAST algorithm. The homologues for SEQ ID NO: 1-113 from Geneseq are shown in Table 1C below.

TABLE 1C

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
1	T26368	742(117.4bits)	5.7e-27	92	T26368 Human gene signature HUMGS08609. Length = 421
2	Z44744	552(88.9bits)	1.9e-19	59	Z44744 Human KLIMP cDNA. Length = 3930

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
3	X84987	2610(397.7bits)	5.7e-127	77	X84987 Human secreted protein gene No. 55. Length = 1182
6	C26589	1680(258.1bits)	3.3e-70	96	C26589 Human secreted protein 5' EST, SEQ ID NO: 30664. Length = 364
7	A45397	1422(219.4bits)	1.7e-58	97	A45397 Human secreted expressed sequence tag SEQ ID NO:1972. Length = 326
8	C10077	1398(215.8bits)	1.5e-57	88	C10077 Human secreted protein 5' EST, SEQ ID NO: 14152. Length = 436
9	V38687	5115(773.5bits)	3.6e-226	82	V38687 Mus musculus SOCS14 cDNA. Length = 2438
10	V68408	8232(1241.2bits)	0.0	98	V68408 Human BAZ1-beta cDNA #1. Length = 5561
11	V88506	2957(449.7bits)	4.8e-127	98	V88506 EST clone FK235. Length = 631
12	T94108	457(74.6bits)	3.1e-14	63	T94108 Human PKD1 locus between chromosomal markers ATP6 (ATP6C) and D16S84.
15	A51727	2762(420.5bits)	4.3e-158	94	A51727 Human nuclear dual-specificity phosphatase cDNA. Length = 4641
16	V68588	8500(1281.4bits)	0.0	91	V68588 Nucleotide sequence encoding the human nuclear protein. Length = 2090
18	C04501	1063(165.5bits)	5.7e-42	93	C04501 Human secreted protein

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					5' EST, SEQ ID NO: 8576. Length = 398
19	A42431	625(99.8bits)	2.3e-21	88	A42431 Human secreted expressed sequence tag SEQ ID NO:1171. Length = 314
23	T26203	929(145.4bits)	2.3e-35	95	T26203 Human gene signature HUMGS08442. Length = 202
24	Z52469	924(144.7bits)	5.4e-66	95	Z52469 HTRM clone 2284580 DNA sequence. Length = 1635
25	Z51477	1738(266.8bits)	6.2e-83	77	Z51477 5'end of human hypertension associated transcription factor-1 DNA.
26	C20297	319(53.9bits)	4.1e-08	82	C20297 Human secreted protein 5' EST, SEQ ID NO: 24372. Length = 162
27	C11303	710(112.6bits)	8.5e-25	100	C11303 Human secreted protein 5' EST, SEQ ID NO: 15378. Length = 145
28	C03585	1582(243.4bits)	1.3e-64	99	C03585 Human secreted protein 5' EST, SEQ ID NO: 3583. Length = 322
29	C03585	1582(243.4bits)	1.3e-64	99	C03585 Human secreted protein 5' EST, SEQ ID NO: 3583. Length = 322
31	X84969	7143(1077.8bits)	1.5e-317	98	X84969 Human secreted protein gene No. 37. Length = 1536
32	Q59401	1803(276.6bits)	9.4e-75	98	Q59401 Human brain Expressed Sequence Tag EST00423. Length = 370

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
33	Z16218	440(72.1bits)	1.6e-14	65	Z16218 Human gene expression product cDNA sequence SEQ ID NO:3688. Length = 767
34	V84575	10934(1646.6bits)	0.0	98	V84575 Human secreted protein gene 165 clone HCDD878. Length = 2379
35	Z51276	1027(160.1bits)	6.3e-65	99	Z51276 Human Polycystic Kidney Disease-2-Like (PKDL) cDNA. Length = 3044
36	X28103	346(58.0bits)	5.5e-06	54	X28103 Freac11 gene. Length = 2106
37	V87189	777(122.6bits)	1.6e-46	98	V87189 EST clone BN130. Length = 338
39	V58761	7265(1096.1bits)	0.0	96	V58761 Human secreted protein cw1233_3 cDNA. Length = 2501
40	C04683	1975(302.4bits)	1.4e-83	99	C04683 Human secreted protein 5' EST, SEQ.ID NO: 8758. Length = 400
41	X23519	393(65.0bits)	4.8e-17	69	X23519 Human kidney aminopeptidase P genomic DNA fragment 3. Length = 44,453
42	A09157	18217(2739.3bits)	0.0	99	A09157 Human cancer associated antigen precursor DNA, clone MO-REN-46.
43	Q39793	480(78.1bits)	1.3e-14	86	Q39793 Expressed Sequence Tag human gene marker EST00140. Length = 327



SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
44	Z65096	11163(1680.9bits)	0.0	99	Z65096 Membrane-bound protein PRO1287 encoding cDNA. Length = 3877
45	A42799	1217(188.6bits)	3.3e-49	95	A42799 Human secreted expressed sequence tag SEQ ID NO:1539. Length = 298
48	T23378	1678(257.8bits)	2.0e-68	94	T23378 Human gene signature HUMGS05205. Length = 386
49	Z97094	5232(791.1bits)	4.1e-231	98	Z97094 Human secreted protein gene 76 cDNA clone HEPCU48, SEQ ID NO:86.
50	Z42186	2555(389.4bits)	4.6e-110	99	Z42186 Human normal bladder tissue cDNA derived EST 65. Length = 806
51	C02784	1914(293.2bits)	2.6e-79	93	C02784 Human secreted protein 5' EST, SEQ ID NO: 2782. Length = 437
52	Z65038	1664(255.7bits)	2.7e-70	77	Z65038 Membrane-bound protein PRO1108 encoding cDNA. Length = 2359
53	X40335	1385(213.9bits)	6.7e-55	99	X40335 Human secreted protein 5' EST SEQ ID NO:122. Length = 283
54	X12619	910(142.6bits)	1.3e-34	95	X12619 Human biallelic polymorphic DNA fragment WI- 21342d. Length = 200
55	C29489	525(84.8bits)	1.3e-16	81	C29489 Human secreted protein 5' EST, SEQ ID NO: 33564. Length = 169
56	A35003	1556(239.5bits)	7.0e-64	74	A35003 Human adenosine

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					receptor related polynucleotide SEQ ID NO:2692.
57	X25445	6227(940.4bits)	3.1e-276	97	X25445 Human PRO216 cDNA clone UNQ265. Length = 1650
58	V24559	953(149.0bits)	5.4e-37	66	V24559 Leukocyte specific protein, Sp140, coding sequence. Length = 2905
59	C16531	642(102.4bits)	6.8e-23	97	C16531 Human secreted protein 5' EST, SEQ ID NO: 20606. Length = 136
60	Z96804	5245(793.0bits)	1.1e-231	98	Z96804 Nuclear transport protein clone hfb066 coding sequence. Length = 1101
61	Z52454	7307(1102.4bits)	0.0	99	Z52454 HTRM clone 003256 DNA sequence. Length = 2186
63	V89203	836(131.5bits)	3.4e-32	70	V89203 EST. clone CJ77. Length = 469
65	X22111	4264(645.8bits)	3.2e-311	98	X22111 Human secreted protein gene 1 clone HTXBK30. Length = 1725
66	Z33338	4754(719.3bits)	1.7e-209	97	Z33338 Human secreted protein clone qb56_19 nucleotide sequence SEQ ID NO:45.
67	X26880	372(61.9bits)	8.2e-18	56	X26880 DNA encoding a protein with cation transporting activity. Length = 1831
68	T26194	1308(202.3bits)	3.8e-52	91	T26194 Human gene signature HUMGS08432. Length = 349

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
69	Z15435	1974(302.2bits)	8.5e-84	98	Z15435 Human gene expression product cDNA sequence SEQ ID NO:2904. Length = 750
70	C01285	2772(422.0bits)	1.4e-118	99	C01285 Human secreted protein 5' EST, SEQ ID NO: 1283. Length = 557
71	Z93373	5355(809.5bits)	6.7e-237	96	Z93373 Sequence encoding F-box protein FBP-23. Length = 1866
73	C01770	822(129.4bits)	3.0e-31	92	C01770 Human secreted protein 5' EST, SEQ ID NO: 1768. Length = 230
74	A29638	1998(305.8bits)	3.3e-136	67	A29638 Human apoptosis related protein ABP130 encoding cDNA SEQ ID NO:5.
75	V84573	2157(329.7bits)	2.0e-92	94	V84573 Human secreted protein gene 163 clone HBMTY28. Length = 1758
77	V87235	463(75.5bits)	1.0e-14	79	V87235 EST clone BO194. Length = 497
78	X58060	2971(451.8bits)	6.3e-128	95	X58060 Genomic DNA for Human GABAB receptors. Length = 16,862
79	C09384	1158(179.8bits)	1.8e-46	98	C09384 Human secreted protein 5' EST, SEQ ID NO: 13459. Length = 252
80	A47439	765(120.8bits)	2.0e-29	100	A47439 Sequence encoding human neuron-associated protein. Length = 1293
81	V40885	2855(434.4bits)	1.8e-122	99	V40885 Coding sequence of clone CC247_10.

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					Length = 625
82	A23438	6158(930.0bits)	0.0	88	A23438 cDNA encoding human secreted protein vc46_1, SEQ ID NO:31. Length = 2880
83	X25081	609(97.4bits)	3.2e-22	69	X25081 Potato tuber-specific ADP-ribosylation factor-1 cDNA clone 10-1.
84	A49187	13844(2083.2bits)	0.0	96	A49187 cDNA encoding human GTPase associated protein-17. Length = 3150
85	V25979	1860(285.1bits)	2.7e-95	96	V25979 Human CD33-like protein encoding cDNA. Length = 2027
87	Z50904	1009(157.4bits)	4.8e-57	74	Z50904 Human TBC-1 partial genomic DNA comprising 5' end sequence. Length = 17,590
88	A34983	432(70.9bits)	4.3e-13	86	A34983 Human adenosine receptor related polynucleotide SEQ ID NO:2672.
89	C28163	294(50.2bits)	1.1e-06	67	C28163 Human secreted protein 5' EST, SEQ ID NO: 32238. Length = 298
90	C04883	903(141.5bits)	2.9e-34	98	C04883 Human secreted protein 5' EST, SEQ ID NO: 8958. Length = 186
92	Z96802	3186(484.1bits)	9.3e-166	97	Z96802 Nuclear transport protein clone hfb060-1 coding sequence. Length = 984
93	C26255	400(66.1bits)	8.9e-12	95	C26255 Human secreted protein 5' EST, SEQ ID NO: 30330. Length = 89

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
94	A11282	2394(365.2bits)	2.2e-103	66	A11282 Rat MAGUIN 1 coding sequence. Length = 3099
95	X61462	2109(322.5bits)	2.1e-112	94	X61462 DNA encoding a human secreted protein. Length = 827
96	X19548	12063(1816.0bits)	0.0	92	X19548 Human lysophosphatidic acid acyltransferase encoding cDNA. Length = 3192
97	Z29233	10265(1546.2bits)	0.0	99	Z29233 Human cell signalling protein-12 encoding cDNA. Length = 2419
99	C01704	1040(162.1bits)	2.2e-59	92	C01704 Human secreted protein 5' EST, SEQ ID NO: 1702. Length = 411
100	V10126	4233(641.2bits)	6.9e-186	98	V10126 Human eosinophil-derived basic protein EBPH cDNA. Length = 865
101	Z23903	353(59.0bits)	1.6e-09	67	Z23903 Human LOBO homologue genomic DNA fragment 5. Length = 49,999
102	A43926	771(121.7bits)	1.7e-27	95	A43926 Human secreted expressed sequence tag SEQ ID NO:501. Length = 182
103	C30718	969(151.4bits)	6.8e-38	97	C30718 Human secreted protein 5' EST, SEQ ID NO: 34793. Length = 233
104	C03663	1771(271.8bits)	2.6e-74	97	C03663 Human secreted protein 5' EST, SEQ ID NO: 3661. Length = 366

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
105	X82085	2104(321.7bits)	3.1e-240	92	X82085 Human SIGP encoding DNA (clone ID 1880830). Length = 1454
106	A43403	1006(157.0bits)	6.1e-40	77	A43403 Rat secreted expressed sequence tag SEQ ID NO:2143. Length = 553
108	A44450	740(117.1bits)	8.0e-28	96	A44450 Human secreted expressed sequence tag SEQ ID NO:1025. Length = 438
109	Z10752	392(64.9bits)	2.7e-11	70	Z10752 Genomic sequence of the human HKNG1 gene. Length = 72,604
110	Z36325	5950(898.8bits)	0.0	89	Z36325 Mechanical stress induced cDNA encoding protein 274. Length = 10,427
111	A44655	1670(256.6bits)	8.7e-70	95	A44655 Human secreted expressed sequence tag SEQ ID NO:1230. Length = 396
112	C19966	1221(189.2bits)	2.7e-49	99	C19966 Human secreted protein 5' EST, SEQ ID NO: 24041. Length = 246
113	C03898	2177(332.7bits)	9.4e-93	97	C03898 Human secreted protein 5' EST, SEQ ID NO: 3896. Length = 463

The homologous sequences to SEQ ID NO: 1-113 were also obtained by a BLASTN version 2.0al 19MP-WashU search against the NCBI Genbank nt database

updated November 10, 2000, using the BLAST algorithm. The homologues for SEQ ID NO: 1-113 from Genbank are shown in Table 1D below.

TABLE 1D

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
1	AK024451.1	6401(966.5bits)	1.7e-283	86	AK024451 Homo sapiens mRNA for FLJ00043 protein, partial cds Length = 4421
2	U89264.1	529(85.4bits)	4.3e-22	61	DMU89264 Drosophila melanogaster kinesin like protein 67a mRNA, complete cds
3	AK001122.1	840(132.1bits)	2.0e-49	66	AK001122 Homo sapiens cDNA FLJ10260 fis, clone HEMBB1000973, moderately similar to Mus musculus schlafen3 mRNA
4	AK001122.1	767(121.1bits)	1.5e-47	67	AK001122 Homo sapiens cDNA FLJ10260 fis, clone HEMBB1000973, moderately similar to Mus musculus schlafen3 mRNA
6	U48972.1	1656(254.5bits)	7.2e-68	71	MMU48972 Mus musculus spindlin (Spin) mRNA, complete cds Length = 4116
8	X03557.1	4486(679.1bits)	1.5e-196	80	HSIF156R Human mRNA for 56-KDa protein induced by interferon Length = 1642
9	AL139316.3	6984(1053.9bits)	0.0	98	CNS01DXH Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC R-698F20 of library RPCI-11 from chromosome 14 of Homo sapiens
10	AC005074.1	8268(1246.6bits)	0.0	98	AC005074 Homo sapiens BAC clone CTA-208H19 from 7q11.23, complete sequence

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
11	AF043117.1	26273(3948.1bits)	0.0	99	AF043117 Homo sapiens ubiquitin-fusion degradation protein 2 (UFD2) mRNA, complete cds
12	AL135818.3	1461(225.3bits)	1.5e-58	88	CNS01DVH Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC C-2547L24 of library CalTech-D from chromosome 14 of Homo
13	AL035456.26	603(96.5bits)	8.3e-21	92	HS1099D15 Human DNA sequence from clone RP5-1099D15 on chromosome 20 Contains the JAG1 gene encoding Jagged1 (involved in
14	U90126.1	524(84.7bits)	2.3e-13	56	BTU90126 Bos taurus ABC transporter mRNA, complete cds Length = 7709
15	AK022478.1	740(117.1bits)	1.7e-26	94	AK022478 Homo sapiens cDNA FLJ12416 fis, clone MAMMA1003019 Length = 1842
16	AK026670.1	9217(1389.0bits)	0.0	98	AK026670 Homo sapiens cDNA: FLJ23017 fis, clone LNG00879 Length = 1908
17	AK001841.1	5578(843.0bits)	6.8e-246	99	AK001841 Homo sapiens cDNA FLJ10979 fis, clone PLACE1001503 Length = 1675
18	AK026518.1	7538(1137.1bits)	0.0	97	AK026518 Homo sapiens cDNA: FLJ22865 fis, clone KAT02171 Length = 1700
19	AK001885.1	9695(1460.7bits)	0.0	99	AK001885 Homo sapiens cDNA FLJ11023 fis, clone PLACE1003784 Length = 1943
20	AC083862.2	2040(312.1bits)	1.1e-84	95	AC083862 Homo sapiens chromosome 7 clone RP11-134L10, complete sequence



SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
22	AL049843.18	3030(460.7bits)	2.0e-129	95	HSJ392M17 Human DNA sequence from clone RP3-392M17 on chromosome 6p12.3-21.2 Contains a pseudogene similar to ATP6C
23	AF222927.1	8103(1221.8bits)	0.0	95	AF222927 Homo sapiens SAMSN1 (SAMSN1) mRNA, complete cds Length = 1888
24	AC008750.7	2882(438.5bits)	9.7e-123	99	AC008750 Homo sapiens chromosome 19 clone CTD-2616J11, complete sequence
25	L32162.1	2952(449.0bits)	4.8e-131	99	HUMTRFA Homo sapiens transcription factor mRNA, 5' end Length = 1520
26	AF121081.1	2283(348.6bits)	2.4e-97	82	AF121081 Mus musculus cAMP inducible 2 protein (Ci2) mRNA, complete cds
28	AF168132.1	16833(2531.7bits)	0.0	99	AF168132 Homo sapiens RU1 (RU1) mRNA, complete cds Length = 3464
29	AF168132.1	16833(2531.7bits)	0.0	99	AF168132 Homo sapiens RU1 (RU1) mRNA, complete cds Length = 3464
30	AL080141.1	977(152.6bits)	6.7e-49	75	HSM800653 Homo sapiens mRNA; cDNA DKFZp434M183 (from clone DKFZp434M183); partial cds
31	AF154415.1	22660(3406.0bits)	0.0	99	AF154415 Homo sapiens FLASH mRNA, complete cds Length = 6782
32	AK025513.1	9434(1421.5bits)	0.0	96	AK025513 Homo sapiens cDNA: FLJ21860 fis, clone HEP02307 Length = 3997
33	AL035562.14	476(77.5bits)	2.5e-26	69	HS1065O2 Human DNA sequence from clone 1065O2 on chromosome 20p11.21-11.23.

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					Contains a copy of the RPL41 gene for Ribosomal
34	AB018339.1	19368(2912.0bits)	0.0	99	AB018339 Homo sapiens mRNA for KIAA0796 protein, partial cds Length = 3900
35	AF094827.1	1027(160.1bits)	2.0e-64	99	AF094827 Homo sapiens PKD2L mRNA, partial cds Length = 2397
36	AB031230.1	11934(1796.6bits)	0.0	96	AB031230 Homo sapiens PCCX2 mRNA for protein containing CXXC domain 2, partial cds
37	AC009477.4	4349(658.6bits)	1.9e-205	97	AC009477 Homo sapiens BAC clone RP11-209H16 from 2, complete sequence
38	AF121081.1	1200(186.1bits)	3.2e-47	75	AF121081 Mus musculus cAMP inducible 2 protein (Ci2) mRNA, complete cds
39	AK022734.1	10265(1546.2bits)	0.0	99	AK022734 Homo sapiens cDNA FLJ12672 fis, clone NT2RM4002339 Length = 2223
40	AL031774.1	5832(881.1bits)	0.0	95	HS298J15 Human DNA sequence from clone 298J15 on chromosome 6p22.3-23 Contains dek (putative oncogene), EST, GSS, CA repeat,
41	AP000316.1	511(82.7bits)	1.2e-15	65	AP000316 Homo sapiens genomic DNA, chromosome 21q22.1, D21S226-AML region, clone:S185, complete sequence
42	AB011121.1	18217(2739.3bits)	0.0	99	AB011121 Homo sapiens mRNA for KIAA0549 protein, partial cds Length = 4745
43	AF143536.1	6097(920.8bits)	2.1e-269	83	AF143536 Homo sapiens colon cancer-associated protein Mic1 (MIC1) mRNA, complete cds

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
44	AK002126.1	13375(2012.8bits)	0.0	100	AK002126 Homo sapiens cDNA FLJ11264 fis, clone PLACE1009111 Length = 2675
45	AB046837.1	1230(190.6bits)	2.1e-48	86	AB046837 Homo sapiens mRNA for KIAA1617 protein, partial cds Length = 4259
46	AC006461.2	1270(196.6bits)	3.5e-138	93	AC006461 Homo sapiens BAC clone RP11-343N14 from 2, complete sequence
47	AL137129.2	452(73.9bits)	1.7e-19	71	CNS01DWE Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC R-618G20 of library RPCI-11 from chromosome 14 of Homo sapiens
48	AB002321.1	25207(3788.1bits)	0.0	99	AB002321 Human mRNA for KIAA0323 gene, partial cds Length = 6227
49	6005839 ref	14820(2229.6bits)	0.0	99	NM_007171.1
50	AL080123.1	7473(1127.3bits)	0.0	98	HSM800631 Homo sapiens mRNA; cDNA DKFZp569D2231 (from clone DKFZp569D2231); partial cds
51	AF227905.1	19241(2893.0bits)	0.0	98	AF227905 Homo sapiens UDP-glucose:glycoprotein glucosyltransferase 1 precursor, mRNA, complete cds
52	AF015811.1	1572(241.9bits)	9.4e-65	76	AF015811 Mus musculus putative lysophosphatidic acid acyltransferase mRNA, complete cds
53	U83115.1	30248(4544.5bits)	0.0	99	HSU83115 Human non-lens beta gamma-crystallin like protein (AIM1) mRNA, partial cds
54	AL033504.3	644(102.7bits)	8.4e-19	65	HS434O8 Human DNA sequence from clone 434O8 on chromosome 6q24.1-25.1. Contains ESTs,

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					an STS and GSSs, complete sequence
55	AF294790.1	1954(299.2bits)	3.8e-82	69	AF294790 Mus musculus RING-finger protein MURF mRNA, complete cds
56	AC006545.3	2019(309.0bits)	9.2e-84	79	AC006545 Homo sapiens chromosome 18q11 clone p1-1028, complete sequence
57	AF282618.1	7508(1132.6bits)	0.0	97	AF282618 Homo sapiens serine carboxypeptidase 1 precursor protein (HSCP1) mRNA, complete cds
58	AK023116.1	725(114.8bits)	2.2e-44	71	AK023116 Homo sapiens cDNA FLJ13054 fis, clone NT2RP3001527, highly similar to Human Sp140 protein (Sp140) mRNA
59	AK023794.1	4002(606.5bits)	4.6e-175	98	AK023794 Homo sapiens cDNA FLJ13732 fis, clone PLACE3000145, moderately similar to TENSIN
60	AK001609.1	11047(1663.5bits)	0.0	99	AK001609 Homo sapiens cDNA FLJ10747 fis, clone NT2RP3001799 Length = 2242
61	AF119869.1	8029(1210.7bits)	0.0	99	AF119869 Homo sapiens PRO2249 mRNA, complete cds Length = 1658
62	AL355305.9	3081(468.3bits)	0.0	98	AL355305 Human DNA sequence from clone RP11-487F23 on chromosome 6, complete sequence [Homo sapiens]
63	AK026003.1	770(121.6bits)	1.2e-27	71	AK026003 Homo sapiens cDNA: FLJ22350 fis, clone HRC06313 Length = 2589
65	Y14591.1	394(65.2bits)	3.1e-07	58	HSFUSION Viral-cellular fusion mRNA with Human papillomavirus type 68 E6 and E7 genes, and

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					Homo sapiens APM-1 gene
66	AC005412.6	462(75.4bits)	2.0e-10	70	AC005412 Homo sapiens chromosome 17, clone hRPK.22_N_12, complete sequence
67	AC002464.1	2683(408.6bits)	1.2e-255	92	AC002464 Human BAC clone CTA-331P3, complete sequence [Homo sapiens]
68	AB023139.1	9024(1360.0bits)	0.0	97	AB023139 Homo sapiens mRNA for KIAA0922 protein, partial cds Length = 2505
69	AJ011863.1	12947(1948.6bits)	0.0	97	HSA011863 Homo sapiens mRNA for homeobox protein LSX Length = 2806
70	AL110222.1	14259(2145.5bits)	0.0	99	HSM800878 Homo sapiens mRNA; cDNA DKFZp434K233 (from clone DKFZp434K233); partial cds
71	AL022395.2	2941(447.3bits)	0.0	95	HS273N12 Human DNA sequence from clone 273N12 on chromosome 6q16.1-16.3. Contains the gene for the N-Oct5a (N-Oct3, N-Oct5b)
72	AB011178.1	13545(2038.3bits)	0.0	93	AB011178 Homo sapiens mRNA for KIAA0606 protein, partial cds Length = 3580
73	AJ278735.1	939(146.9bits)	2.1e-35	71	MMU278735 Mus musculus mRNA for hypothetical protein (ORF1), 1975 BP
74	AF274863.1	20922(3145.2bits)	0.0	98	AF274863 Homo sapiens secretory pathway component Sec31B-1 mRNA, alternatively spliced, complete cds
75	AF223466.1	4292(650.0bits)	2.0e-229	96	AF223466 Homo sapiens HT015 protein (HT015) mRNA, complete cds Length = 1429

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
77	Y14383.1	1962(300.4bits)	5.7e-82	96	HSY14383 Homo sapiens gamma adducin gene, exon 13 Length = 421
78	AC006137.2	2975(452.4bits)	6.1e-127	96	AC006137 Homo sapiens clone SCb-254N2 (UWGC:rg254N02) from 6p21, complete sequence
79	AB020860.1	1218(188.8bits)	1.5e-53	98	AB020860 Homo sapiens genomic DNA of 8p21.3-p22 anti-oncogene of hepatocellular colorectal and non-small cell lung cancer ,
80	AB041648.1	681(108.2bits)	9.3e-24	92	AB041648 Mus musculus brain cDNA, clone MNCb-0091 Length = 1835
81	AB032976.1	22422(3370.3bits)	0.0	98	AB032976 Homo sapiens mRNA for KIAA1150 protein, partial cds Length = 5051
82	AK000539.1	1889(289.5bits)	2.4e-160	96	AK000539 Homo sapiens cDNA FLJ20532 fis, clone KAT10877 Length = 1135
83	AF119889.1	2770(421.7bits)	4.8e-119	90	AF119889 Homo sapiens PRO2667 mRNA, complete cds Length = 1586
84	AL117448.1	22230(3341.4bits)	0.0	97	HSM800958 Homo sapiens mRNA; cDNA DKFZp586B1417 (from clone DKFZp586B1417); partial cds
85	AC018755.3	1407(217.2bits)	3.0e-119	99	AC018755 Homo sapiens chromosome 19, BAC BC330783 (CIT-HSPC_470E3), complete sequence
87	U49974.1	1364(210.7bits)	1.2e-90	83	HSU49974 Human mariner2 transposable element, complete consensus sequence
88	X80240.1	1477(227.7bits)	1.7e-59	84	HSERVKC4 Homo sapiens endogenous retrovirus HERV-KC4 DNA Length = 6369

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
89	AC007969.3	408(67.3bits)	1.3e-08	61	AC007969 Homo sapiens BAC clone RP11-471A5 from 2, complete sequence
90	AL158040.13	6205(937.0bits)	5.1e-315	100	AL158040 Human DNA sequence from clone RP11-360G10 on chromosome 10 Contains parts of the genes for two novel proteins,
91	AL133372.2	742(117.4bits)	1.9e-32	67	CNS01DUX Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC R-269C4 of library RPCI-11 from chromosome 14 of Homo sapiens
92	AL050345.1	3030(460.7bits)	1.8e-190	97	HS508115A Novel human gene mapping to chromosome 22 Length = 1111
94	AB020709.1	2445(372.9bits)	1.4e-104	65	AB020709 Homo sapiens mRNA for KIAA0902 protein, complete cds Length = 4349
95	AL080201.1	2109(322.5bits)	4.3e-179	94	HSM800726 Homo sapiens mRNA; cDNA DKFZp434F162 (from clone DKFZp434F162); partial cds
96	AL079352.3	3640(552.2bits)	4.1e-312	87	CNS00M8V Human chromosome 14 DNA sequence *** IN PROGRESS *** BAC R-388G3 of library RPCI-11 from chromosome 14 of Homo sapiens
97	Y14153.1	10120(1524.5bits)	0.0	99	HSBTRCP Homo sapiens mRNA for beta-transducin repeat containing protein
99	AC005318.1	7228(1090.5bits)	0.0	96	AC005318 Homo sapiens Chromosome 15q26.1 PAC clone pDJ105i19, complete sequence
100	AF132209.2	4193(635.2bits)	4.7e-183	98	AF132209 Homo sapiens prepro-major basic protein homolog

SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					mRNA, complete cds
101	AC008444.4	464(75.7bits)	1.6e-13	67	AC008444 Homo sapiens chromosome 5 clone CTC-338N15, complete sequence
102	AK024431.1	10307(1552.5bits)	0.0	97	AK024431 Homo sapiens mRNA for FLJ00020 protein, partial cds Length = 4319
103	AL022240.8	2425(369.9bits)	4.2e-102	92	HS328E19 Human DNA sequence from clone 328E19 on chromosome 1q12-21.2 Contains a cyclophilin-like gene, a novel gene, ESTs,
104	AL109827.8	726(115.0bits)	7.5e-31	73	HSJ309K20 Human DNA sequence from clone RP1-309K20 on chromosome 20. Contains the gene for a novel protein similar to
105	AL137727.1	14696(2211.0bits)	0.0	98	HSM802274 Homo sapiens mRNA; cDNA DKFZp434M0519 (from clone DKFZp434M0519); partial cds
106	X53777.1	1098(170.8bits)	6.1e-62	79	HSL23MR Human L23 mRNA for putative ribosomal protein Length = 770
109	AL133245.2	1911(292.8bits)	7.1e-79	97	CNS01DUI BAC sequence from the SPG4 candidate region at 2p21-2p22 BAC 854M03 of RPCI-11 library from chromosome 2 of Homo
110	AB037728.1	22325(3355.7bits)	0.0	99	AB037728 Homo sapiens mRNA for KIAA1307 protein, partial cds Length = 5601
111	AB046853.1	1500(231.1bits)	1.3e-60	92	AB046853 Homo sapiens mRNA for KIAA1633 protein, partial cds Length = 5054
112	AL354696.11	1229(190.4bits)	4.2e-98	98	AL354696 Human DNA sequence from



SEQ ID NO:	ACCESSION NO	BLAST SCORE	P-VALUE	% IDENTITY	DESCRIPTION
					clone RP11-74J13 on chromosome 13, complete sequence [Homo sapiens]
113	AK000874.1	6628(1000.5bits)	0.0	98	AK000874 Homo sapiens cDNA FLJ10012 fis, clone HEMBA1000307 Length = 1901

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), the

5 polypeptide sequences corresponding to SEQ ID NO: 1-113 were examined to determine whether they had identifiable signature regions. Table 2 shows the signature region found in the indicated polypeptide sequences, the description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

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TABLE 2

SEQ ID NO:	P-VALUE	EMATRIX SCORE	ACCESSION NO	DESCRIPTION	RESIDUES
2	5.235e-23	15.66	BL00411H	Kinesin motor domain proteins.	36-67
2	1.978e-16	9.93	PR00380D	KINESIN HEAVY CHAIN SIGNATURE	37-59
3	8.615e-09	12.74	BL00113A	Adenylate kinase proteins	484-501
9	7.805e-12	9.13	PR00678H	PI3 KINASE P85 REGULATORY SUBUNIT SIGNATURE	165-188
10	7.136e-12	13.82	BL00633B	Bromodomain proteins	404-429
10	8.773e-12	15.84	PF00628	PHD-finger	267-282
10	1.750e-11	20.81	PR00503D	BROMODOMAIN SIGNATURE	437-457
10	9.640e-11	9.96	PR00503B	BROMODOMAIN SIGNATURE	403-420
11	2.125e-09	3.12	BL00115Z	Eukaryotic RNA polymerase II heptapeptide repeat proteins	354-403
11	4.309e-09	3.12	BL00115Z	Eukaryotic RNA polymerase II heptapeptide repeat proteins	319-368
13	9.455e-11	15.11	BL00636B	Nt-dnaJ domain proteins	8-29
13	5.632e-10	13.48	PR00625B	DNAJ PROTEIN FAMILY SIGNATURE	8-29

SEQ ID NO:	P-VALUE	EMATRIX SCORE	ACCESSION NO	DESCRIPTION	RESIDUES
16	3.118e-10	9.88	PR00891F	RAB GDI/REP PROTEIN FAMILY SIGNATURE	162-180
18	9.830e-21	12.60	PR00193C	MYOSIN HEAVY CHAIN SIGNATURE	177-205
18	2.212e-18	11.69	PR00193B	MYOSIN HEAVY CHAIN SIGNATURE	125-151
18	5.925e-12	15.41	PR00193A	MYOSIN HEAVY CHAIN SIGNATURE	65-85
18	9.031e-10	10.66	BL00567A	Phosphoribulokinase proteins	127-146
25	7.279e-31	19.43	PD01066	PROTEIN ZINC FINGER ZINC-FINGER METAL-BINDING NU	81-120
26	5.438e-09	15.07	BL00942F	glpT family of transporters proteins	159-177
31	3.778e-09	23.85	BL00434C	HSF-type DNA-binding domain proteins	4-44
31	7.360e-09	8.23	PR00554E	ADENOSINE A2B RECEPTOR SIGNATURE	731-743
32	1.771e-10	12.19	PR00320B	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	123-138
32	6.824e-10	16.74	PR00320A	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	123-138
32	3.842e-09	9.67	BL00678	Trp-Asp (WD) repeat proteins proteins	125-136
32	7.300e-09	13.01	PR00320C	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	123-138
34	4.869e-09	16.74	PD02102A	SUBUNIT E V-ATPASE VACUOLAR ATP SYNTHASE HYDROL	339-383
49	6.880e-09	9.83	BL00724B	Stress-induced proteins SRP1/TIP1 family proteins	99-122
50	6.786e-13	10.52	PR00048A	C2H2-TYPE ZINC FINGER SIGNATURE	137-151
50	8.714e-13	10.52	PR00048A	C2H2-TYPE ZINC FINGER SIGNATURE	165-179
50	9.500e-13	13.92	PD00066	PROTEIN ZINC-FINGER METAL-BINDI	156-169
50	5.696e-12	16.07	BL00028	Zinc finger, C2H2 type, domain proteins	168-185
50	1.000e-09	16.07	BL00028	Zinc finger, C2H2 type, domain proteins	140-157
50	1.600e-09	13.92	PD00066	PROTEIN ZINC-FINGER METAL-BINDI	128-141
53	7.517e-24	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	622-657

SEQ ID NO:	P-VALUE	EMATRIX SCORE	ACCESSION NO	DESCRIPTION	RESIDUES
53	8.297e-20	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	804-839
53	2.575e-19	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	713-748
53	8.200e-19	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	515-550
53	4.808e-14	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	413-448
53	5.500e-14	18.06	BL00225B	Crystallins beta and gamma 'Greek key' motif proteins	894-929
53	5.829e-12	13.82	BL00225A	Crystallins beta and gamma 'Greek key' motif proteins	860-881
53	3.127e-09	13.82	BL00225A	Crystallins beta and gamma 'Greek key' motif proteins	576-597
57	8.833e-15	29.13	BL00131G	Serine carboxypeptidases, serine proteins	101-138
57	8.714e-13	17.66	BL00131F	Serine carboxypeptidases, serine proteins	49-75
60	8.703e-10	19.54	BL01160B	Kinesin light chain repeat proteins	146-200
60	2.373e-09	19.54	BL01160B	Kinesin light chain repeat proteins	153-207
65	2.957e-12	16.07	BL00028	Zinc finger, C2H2 type, domain proteins	151-168
65	3.100e-09	13.92	PD00066	PROTEIN ZINC-FINGER METAL-BINDI	167-180
67	3.676e-10	21.17	DM00973A	3 kw RESISTANCE BENOMYL YLL028W CYCLOHEXIMIDE	181-218
67	9.864e-09	9.63	PR00258B	SPERACT RECEPTOR SIGNATURE	142-154
70	9.504e-09	9.10	PF00624I	Flocculin repeat proteins	601-631
72	4.687e-11	26.52	BL01032F	Protein phosphatase 2C proteins	553-593
72	8.000e-09	11.19	PR00019A	LEUCINE-RICH REPEAT SIGNATURE	327-341
75	8.412e-10	15.82	BL00215A	Mitochondrial energy transfer proteins	16-41
94	7.968e-09	16.20	BL00790R	Receptor tyrosine kinase class V proteins	29-73
95	4.000e-10	16.07	BL00028	Zinc finger, C2H2 type, domain proteins	85-102
95	5.304e-10	10.52	PR00048A	C2H2-TYPE ZINC FINGER SIGNATURE	82-96

SEQ ID NO:	P-VALUE	EMATRIX SCORE	ACCESSION NO	DESCRIPTION	RESIDUES
97	6.870e-13	12.19	PR00320B	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	464-479
97	7.429e-13	16.74	PR00320A	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	464-479
97	9.217e-13	12.19	PR00320B	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	341-356
97	2.000e-12	13.01	PR00320C	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	464-479
97	2.500e-12	13.01	PR00320C	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	504-519
97	3.769e-12	12.19	PR00320B	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	424-439
97	4.103e-11	16.74	PR00320A	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	381-396
97	4.194e-11	12.19	PR00320B	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	504-519
97	4.724e-11	16.74	PR00320A	G-PROTEIN BETA WD-40 REPEAT SIGNATURE	424-439
99	5.500e-13	17.87	BL01133A	Uncharacterized protein family UPF0017 proteins	244-260
100	9.200e-15	12.19	PR00770C	EOSINOPHIL MAJOR BASIC PROTEIN SIGNATURE	112-129
100	7.000e-11	13.71	PR00770A	EOSINOPHIL MAJOR BASIC PROTEIN SIGNATURE	3-27
100	7.047e-11	11.43	PR00770B	EOSINOPHIL MAJOR BASIC PROTEIN SIGNATURE	91-107
100	8.500e-09	16.68	BL00615A	C-type lectin domain proteins	111-129
104	7.000e-09	14.39	BL00030A	Eukaryotic RNA-binding region RNP-1 proteins	69-88
112	3.483e-09	22.53	PD00126A	PROTEIN REPEAT DOMAIN TPR NUCLEA	87-108
113	2.245e-10	16.70	PD02474A	SYNTHASE SMALL SUBUNIT ACETOLACT	138-180

Using the PFam software program (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1) pp. 320-322 (1998) herein incorporated by reference) all the polypeptide sequences

corresponding to SEQ ID NO: 1 – 113 were examined for domains with homology to certain peptide domains. Table 3 shows the name of the domain found, the description, the e-value and the Pfam score for the identified domain within the sequence.

5

TABLE 3

SEQ ID NO:	PFAM MODEL NAME	ACCESSION NO	PFAM SCORE	E-VALUE
2	Kinesin	PF00225	101.3	4.5e-27
3	Viral_helicase1	PF01443	7.6	0.23
7	Ribosomal_S8	PF00410	2.9	8.2
8	TPR	PF01365	12.7	2.1
8	TPR	PF01365	10.1	3.9
8	TPR	PF01365	11.1	3.1
9	SH2	PF00017	18.0	5.6e-05
10	bromodomain	PF00439	72.5	1.2e-19
10	Hemagglutinin	PF00509	-0.3	7.8
10	PHD	PF00628	38.8	1.3e-07
10	zf-B_box	PF00643	-3.3	7.4
11	E1_N	PF00524	5.0	2.1
11	MHC I	PF00129	3.7	7.3
16	OKR_DC_1	PF01276	4.7	1.3
18	myosin_head	PF00063	169.6	1.4e-48
18	PRK	PF00485	4.7	2.3
25	KRAB	PF01352	107.1	3.4e-28
27	zf-C3HC4	PF00097	20.8	4.2e-05
31	bZIP	PF00170	10.4	0.21
32	WD40	PF00400	7.2	6.2
32	WD40	PF00400	32.3	1.1e-05
34	spectrin	PF00435	37.0	8.9e-09
34	spectrin	PF00435	19.6	0.00058
34	spectrin	PF00435	5.6	4.4
34	spectrin	PF00435	32.4	1.7e-07
34	spectrin	PF00435	0.1	1.5e+02
34	spectrin	PF00435	51.8	7e-13
36	F-box	PF00646	13.2	0.66
36	PHD	PF00628	1.4	0.057
38	granulin	PF00396	4.1	6.5
45	Ephrin	PF00812	3.7	7.3
48	Collagen	PF01391	-49.8	1.1
49	FecCD_family	PF01032	-220.7	9.4
50	zf-C2H2	PF00096	30.1	5.2e-05
50	zf-C2H2	PF00096	14.0	3.6
52	Matrix	PF00661	4.2	1.5
52	SH2	PF00017	3.6	5.7
53	Ricin_B_lectin	PF00652	14.1	0.0041
53	crystall	PF00030	30.9	9.1e-06
53	crystall	PF00030	97.2	3.3e-25
53	crystall	PF00030	64.5	2.2e-15
53	crystall	PF00030	61.8	1.5e-14
53	crystall	PF00030	85.9	8.3e-22
57	serine_carbpept	PF00450	72.7	4.3e-19

SEQ ID NO:	PFAM MODEL NAME	ACCESSION NO	PFAM SCORE	E-VALUE
61	kinesin	PF00225	5.2	1.7
65	zf-C2H2	PF00096	30.8	3.1e-05
65	zf-C2H2	PF00096	14.9	1.9
65	zf-C2H2	PF00096	16.8	0.52
65	zf-C2H2	PF00096	2.6	57
72	LRR	PF00560	7.6	78
72	LRR	PF00560	4.2	2.5e+02
72	LRR	PF00560	5.8	1.4e+02
72	PP2C	PF00481	79.0	1.8e-21
72	LRR	PF00560	14.8	2.1
72	LRR	PF00560	0.8	7.7e+02
72	LRR	PF00560	4.7	2e+02
72	LRR	PF00560	8.9	50
72	LRR	PF00560	9.8	36
72	LRR	PF00560	4.6	2.1e+02
72	LRR	PF00560	3.8	2.9e+02
72	LRR	PF00560	11.0	24
72	LRR	PF00560	1.2	6.9e+02
72	LRR	PF00560	20.6	0.038
72	LRR	PF00560	14.1	3.4
72	LRR	PF00560	14.3	2.9
74	GST	PF00043	4.2	2.9
74	WD40	PF00400	28.5	0.00016
74	WD40	PF00400	1.6	35
74	WD40	PF00400	8.2	4.6
74	WD40	PF00400	6.3	8.2
75	mito_carr	PF00153	19.6	7.1e-05
84	DENN	PF02141	159.8	4.7e-44
87	Transposase_1	PF01359	-32.3	6.4
94	SAM	PF00536	28.7	0.00014
95	zf-C2H2	PF00096	7.6	20
95	zf-C2H2	PF00096	13.0	6.1
95	zf-C2H2	PF00096	30.0	5.7e-05
97	F-box	PF00646	29.6	7.1e-05
97	SAM_PNT	PF02198	-26.9	9.7
97	WD40	PF00400	26.4	0.00067
97	WD40	PF00400	46.6	5.6e-10
97	WD40	PF00400	18.5	0.16
97	WD40	PF00400	42.3	1.1e-08
97	WD40	PF00400	35.9	9.2e-07
97	WD40	PF00400	38.8	1.2e-07
97	WD40	PF00400	28.1	0.00021
104	rrm	PF00076	24.6	0.0024
110	ART	PF01129	2.9	6.8
112	TPR	PF01365	7.7	7.1
112	TPR	PF01365	28.2	0.00019

The polypeptide sequence within each of the polypeptides corresponding to SEQ ID NO: 1-113 that is the predicted signal peptide sequence and its cleavage site can be

determined using Neural Network SignalP V1.1 program (from Center for Biological Sequence Analysis, The Technical University of Denmark). The process for identifying prokaryotic and eukaryotic signal peptides and their cleavage sites are also disclosed by Henrik Nielson, Jacob Engelbrecht, Soren Brunak, and Gunnar von Heijne in the publication "Identification of prokaryotic and eukaryotic signal peptides and prediction of their cleavage sites" Protein Engineering, Vol. 10, no. 1, pp. 1-6 (1997), incorporated herein by reference. A mean S score, as described in the Nielson et. al. was obtained for the polypeptide sequences. Table 4 shows the position of the predicted signal peptide in each of the polypeptides corresponding to SEQ ID NO: 1-113 and the mean score associated with that signal peptide.

TABLE 4

SEQ ID NO:	SIGNAL PEPTIDE POSITION	MEAN SCORE	CUTOFF	CONCLUSION
1	1-246	0.085	0.48	NO
2	1-23	0.293	0.48	NO
3	1-454	0.101	0.48	NO
4	1-97	0.093	0.48	NO
5	1-44	0.325	0.48	NO
6	1-112	0.074	0.48	NO
7	1-133	0.337	0.48	NO
8	1-344	0.062	0.48	NO
9	1-281	0.071	0.48	NO
10	1-400	0.081	0.48	NO
11	1-863	0.123	0.48	NO
12	1-15	0.112	0.48	NO
13	1-19	0.217	0.48	NO
14	1-171	0.144	0.48	NO
16	1-491	0.102	0.48	NO
17	1-357	0.069	0.48	NO
18	1-161	0.102	0.48	NO
19	1-161	0.073	0.48	NO
20	1-16	0.231	0.48	NO
21	1-34	0.736	0.48	YES
22	1-20	0.354	0.48	NO
23	1-36	0.565	0.48	YES
24	1-13	0.243	0.48	NO
25	1-23	0.461	0.48	NO
26	1-58	0.444	0.48	NO
27	1-530	0.049	0.48	NO
28	1-88	0.068	0.48	NO
29	1-88	0.068	0.48	NO
30	1-83	0.154	0.48	NO
31	1-1005	0.042	0.48	NO
32	1-41	0.068	0.48	NO
33	1-27	0.879	0.48	YES
34	1-972	0.081	0.48	NO

SEQ ID NO:	SIGNAL PEPTIDE POSITION	MEAN SCORE	CUTOFF	CONCLUSION
35	1-54	0.181	0.48	NO
36	1-527	0.093	0.48	NO
37	1-17	0.497	0.48	YES
38	1-17	0.497	0.48	YES
39	1-73	0.137	0.48	NO
40	1-71	0.264	0.48	NO
41	1-38	0.510	0.48	YES
42	1-188	0.074	0.48	NO
43	1-130	0.130	0.48	NO
44	1-224	0.084	0.48	NO
45	1-35	0.249	0.48	NO
46	1-21	0.169	0.48	NO
47	1-18	0.514	0.48	YES
48	1-150	0.108	0.48	NO
49	1-682	0.348	0.48	NO
50	1-206	0.050	0.48	NO
51	1-511	0.079	0.48	NO
52	1-114	0.152	0.48	NO
53	1-422	0.058	0.48	NO
54	1-74	0.197	0.48	NO
55	1-211	0.256	0.48	NO
56	1-20	0.705	0.48	YES
57	1-126	0.077	0.48	NO
58	1-70	0.125	0.48	NO
59	1-100	0.139	0.48	NO
60	1-87	0.038	0.48	NO
61	1-262	0.062	0.48	NO
62	1-68	0.073	0.48	NO
63	1-13	0.219	0.48	NO
64	1-48	0.086	0.48	NO
65	1-274	0.052	0.48	NO
66	1-53	0.268	0.48	NO
67	1-203	0.219	0.48	NO
68	1-19	0.322	0.48	NO
69	1-143	0.416	0.48	NO
70	1-139	0.102	0.48	NO
71	1-25	0.674	0.48	YES
72	1-19	0.215	0.48	NO
73	1-21	0.307	0.48	NO
74	1-658	0.108	0.48	NO
75	1-94	0.161	0.48	NO
76	1-127	0.088	0.48	NO
77	1-45	0.087	0.48	NO
78	1-71	0.229	0.48	NO
79	1-21	0.624	0.48	YES
80	1-21	0.400	0.48	NO
81	1-263	0.081	0.48	NO
82	1-39	0.125	0.48	NO
83	1-17	0.234	0.48	NO
84	1-355	0.122	0.48	NO
85	1-125	0.214	0.48	NO
86	1-17	0.099	0.48	NO



SEQ ID NO:	SIGNAL PEPTIDE POSITION	MEAN SCORE	CUTOFF	CONCLUSION
87	1-19	0.108	0.48	NO
88	1-21	0.743	0.48	YES
89	1-69	0.087	0.48	NO
90	1-83	0.281	0.48	NO
91	1-21	0.146	0.48	NO
92	1-27	0.377	0.48	NO
93	1-12	0.206	0.48	NO
94	1-140	0.103	0.48	NO
95	1-13	0.273	0.48	NO
96	1-131	0.210	0.48	NO
97	1-18	0.575	0.48	YES
98	1-81	0.159	0.48	NO
99	1-134	0.166	0.48	NO
100	1-17	0.959	0.48	YES
101	1-16	0.102	0.48	NO
102	1-344	0.076	0.48	NO
103	1-25	0.240	0.48	NO
104	1-159	0.081	0.48	NO
105	1-7	0.103	0.48	NO
106	1-36	0.288	0.48	NO
107	1-30	0.193	0.48	NO
108	1-2	0.058	0.48	NO
109	1-17	0.130	0.48	NO
110	1-111	0.186	0.48	NO
111	1-14	0.149	0.48	NO
112	1-167	0.075	0.48	NO
113	1-84	0.035	0.48	NO

#### 4.4 EXAMPLE 4

##### Assemblage of Novel Nucleic Acids

5           The contigs or nucleic acids of the present invention, designated as SEQ ID NO: 227-339 were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (i.e., Hyseq's database containing EST sequences, dbEST version 114, gb pri 114, and UniGene version 101) that belong to this assemblage. The algorithm  
10 terminated when there was no additional sequences from the above databases that would extend the assemblage. Inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

15           A polypeptide was predicted to be encoded by each of SEQ ID NO: 227-339 as set forth below. The polypeptides was predicted using a software program called FASTY

(available from <http://fasta.bioch.virginia.edu>) which selects a polypeptides based on a comparison of translated novel polynucleotide to known polynucleotides (W.R. Pearson, Methods in Enzymology, 183:63-98 (1990), herein incorporated by reference. The predicted polypeptides, SEQ ID NO: 340-452 are shown in Table 6. These polynucleotides

5 and polypeptides have homology to the sequences selected in Example 3.

TABLE 6

SEQ ID NO:	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E=Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
340	3	1198	TQEIASRDSGVPGLEADTTGIQVKEVGGSEVPETAT GTAETEILGTQEIASRSSGVPGLESEVAGAQETEVG GSGISGPEAGMAEARVLMTRKTEIIVPEAEKEEAQT SGVQEAETRVGSALKYEALRAPVTQPRVLGSQEA EISGVQGSSETQVLRVQEAAGVWGMSEGKSGAWGAQ EAEMKVLES PENKSGTFKAQEAAGV LGNEKGKEAE GSLTEASLPEAQVASGAGAGAPRASSPEKAEDRRL PGSQAPPALVSSSQSLEWCQEVTTGYRGVRI TNFT TSWRNGLAFCAILHRFYPDKIDYAPLDPLNIKQNNK QAFDGF AALGVSRLLEPADMVLLSVPDKLIVMTYLC QIRAFCTGQELQLVQLEGGGGAGTYRVGSAQPSPPF PV
341	103	808	ASSDASGGEPKGVTTVMAVEDSTLQVVVRVPPTP RELDSQRRPVVQVDERVLVFNPEEPDGGFPLKKG GTHDGPKKKGKDLTFVFD RVFGEAATQQDVFOHTTH SVLDSFLQGYNCV FAYGATGAGKTHTMLGREGDPG IMYLTTVELYRRL EARQQEKHFEVLISYQEVYNEQI HDLLEPKGPLAIREDPDKGVVQGLSFHQPASAEQL LEILTRGNRNRTQHPTDAN
342	183	661	IYWCKFNMEANHCSLGVPSYPDLVIDVGEVTLGEE NRKKLQKTQRDQERARVIRAACALLNSGGGV IQMEM ANRDERPTMGLDLEESLRKLIQYPYLQAFFETKQH GRCFYIFVKSWSGDPFLKDG SFNSRICSLSSSLYCR SGTSVLHMNSRSTRP
343	1	460	FRVLAPSLGLRSCVSTRASGSSPAESASGCNSSASF SCEFNM EANCQPLVVPEPSYPDLVINVGEVTLGEENR KKLQKIQRDQEKERVMAACALLNSGGGVIRMAKKV EHTVEMGLDLEQSLREL IQSSDLQAFFETKQGRCF YIFVKSWS
344	349	890	PCQSLFVPLGNWLG PWRIMSGTSSPEAVKKLLENMQ SDLRALSL ECKKKFPPVKEAESGIIKVKTIAARNT EILAALKENSSEGVQPF LMGCGTKPKITQLCLAAI

			QRLMSHEVVSETAAGNIINMLWQLMENSLEELKLLQ TVLVLLTTNTVVHDEALSKVGKLFARVHMCFTVFE
345	511	722	AMSPPTVPPMGVDGVSAYLMKKRHTHRKQRRKPTFL TRRNIVGCRIQHGKKEGNEPVEQWKGTVLDPGIR
346	2	769	APDSDDGSDADSEVGPGSPTRTAEAAEEEMAGPNQL CIRRWTTKHVAVWLKDEGFFEYVDILCNKHLRDLGIT LLTLTEYDLRSPPLEIKVLGDIKRMLSVRKLQKIH IDVLEEMGYNSDSPMGSMTPFISALQSTDWLCNGEL SHDCDGPITDLNSDQYQYMNGKNKHSVRRLDPEYWK TILSCIYVFIVFGFTSFIMVIVHERVPDMQTYPLP DIFLDSVPRIPWAFAMTEVCGMILCYIWLLVLLLHK HRS
347	3	939	KTCFEKALEGNPENPEFNTGYAITVYRLDKFNTASG RNKAFSLHVLKRAVRLNDDVYIRVLLALKLQDEGQ EAEGEKYIEEALTSISSQAYVFQYAAKFYRRKGSVD KALELLKMALETTPTS AFLHHQMGLCYRAQMIQIKE ATNWQPRG\QDRETVDRLVQLAICKFEKTI MLKRTF EMAYVDLAET YAEIGHHRKAEHFQKGLRMKIFEDQ LKQEIHYHYGRFQEHHGKSODKAITHYLKGLKIEKM SHSREKLLNALEKLAKRCIHQNVVSVSLLGLIH KLKGEVSDALLCYERALRLAADLNP
348	1	681	STDLSQTELRDQQLKRRNMEENINCFSTNVQPCVI TTDNALCREGPMGTGSMNLVSNNIEDSDMSDDEI LTLCTSSRKRNKPKWDLDEILQLETPPKYHTQIDY VHCLVPDLLQINNPNPCYWGVMCKYAAEALLEGKPEG TFLLRDSAQEDYLFVSFRYSRSLHARIEQWNHNF SFDADHP*VFHSPDITGLLEHYKDPSACMFFEPILLS TPLIRTFPFCL
349	1	217	GRPTRPKNKENGKVENGGLGKTRKKEIVKFEPQVDT EAEDMISAVKSKRLLAIQAKKEREIQEREMKGKISC *EKGEAL*KNKENGKVENGGLGKTRKKEIVKFEPQV DTEAEDMISAVKSKRLLAIQAKKEREIQEREMKGKI SC
350	2	210	KYRGYLYFAALLFRFFPKALYVDCIFSFSQVKVV EKYFSGPAITLENTRVVSQSLQHYL*LGRVSVQ
351	2	311	TAHL PAPS PATAHL PVSPATAHL PAPS PATAHL PA PSPATAHL PAPS PATAHL PVSPATAHL PAPS PATA HL PAPS PATAHL PVSPATAHL PAPS PATAHL PAPS PATAHL PAPS PATAHL PVSPATAHL PAPS PATAHL PAPS PATAHL PVSPATAHL PAPS PATAHL PAPS PA TAHL PAPS PATAHL PVSPATAHL PAPS PATAHL PA PSPATAHL PVLTCHGPPFHPHLPQLTL
352	3	327	QILGKVYSVLS DREQRAVDEQGTVEDSDPVLTQDR DWEAYWRLLFKKISLEDIAFEKTYKGSEELADIK QAYLDFKGDMDQIMESVLCVQYTEEPRI RNIIQQA
353	1	599	LSRNL DVRAFIYKTLMPSEANGLLNSLLDIVSSLSA LLAKAQHVFEYLPFLHTFKITALLETLDFQVVSQN VQARSSAFGSFQFVMKMKVCKDQASFLSDSNMFINLP RVKELLEDDKEKFNIPEDSTPFCLKYQEILQLPNG ALVWTF LKPI LHGKILYTPNTPEINKVIQKANYTFY IVDKLKTLSSETLLEMSSLF
354	3	267	TIGRQYLLKKKTGTIVEERVNRPGWNEDDDVSVSDE SELPTSTTLKASEKSTMEQLVEKACFRDYQRLGLGT ISGSSSRSPESRRG
355	32	725	TLEFEKEDLMNGVKKEISISIGKKRRCVVFNQGE LDAMEYHTKIRELILDGSLQLIQEGLKSGFLYPLFE

			KQDKGSKPITLPLDACSLSELCEMAKHLPSLNEMEH QTLQLVEEDTSVTEQDLFLRVVENNSSFTKVITLMG QKYLPPKSSFLLSDISCMQPLLNYRKTDFDIVIDP PWQNKSVKRSNRYSYLSPLQIKQIPKLAAPNCLL VTWVTNRQKHLRFIK
356	3	792	DAWADAWDRFVADFKAQGPPKPNTEGGAVLPSCAD LFVYYKKCMVQCSQLSTGEPMIALTTIFQKYLREYA WKILSGNLPKTTTSSGGLTISSLLKEKEGSEVAKFT LEELCLICNILSTAHEYCLATTQOLEEKLEKVDVSL IERINLTGEMDTFSTVISSSIQLLVQDLDAACDPAL TAMSKMQWQNVHVGDSQSPYVTSVILHIKQNVPIIR DNLASTRKYFTQFCVKFANSFIPKFITHLFKCKPIS MVGAEQVRWT
357	3	602	PRCRNSARVADTFYTNAGCTLVALNPFKVPQIYSP ELMREYHAAPQPQKLKPHVFTVGEQTYRNVKSLEP VNQSIVVSGESGAGKTWTSRCLMKFYAVVATSPASW ESHKIAERIEQRILNSNPVMEAFGNACTLRNNSSR FGKFIQLQLNRAQMTGAAVQTYLLEKTRVACQASS ERNKDPPIPELTRLLQSSQ
358	3	762	HEDMSSPGLELPSCELSRLEETAEIVASSLPSPLRR EKLALALENEGYIKLLELFHVCEDELENIEGLHHLY EIIKGIFLLNRTALFEVMFSEECIMDVIGCLEYDPA LSQPRKHREFLTAKTAKFEVIPISDPELKQKIHQTY RVQYIQDMVLTPSVFEENMLSTLHSFIFFNKVEIV GMLQEDEKFLTDLFAQLTDEATDEEKRQELVNFLKE FCAFSQTLQPQNRDAFFKTLNMGILPALEVILGMD
359	1	396	NDPVRSKFCKIRVLCHTLARNMVYILTITTPKSSD SRKRKAVILTARVHPGETNSSWIMKGFIDYILGNSS DAQLLRDTFVFKVVFMLNPDGVIVGNYRCSLAGRDL NRNYTSLLESFSPSVWYTRNMVHR
360	3	816	QEATGLGTSTQPLTSSASSLTGFSNWSAAIAPSSST IINEDASFFHQGGVPAASANNALLFQNFPHVSPG FGGSFSPQIGPLSQHHPHHPHQHHSQHQQRRSP ASPHPPPPFTHRNAAFNQLPHLANNLNKPPSPWSSYQ SPSPTPSSSWSPGGGGYGGWGSQGRDHRRGLNGGI TPLNSISPLKKNFASNHIQLQKYARPSSAFAPKSWM EDSLNRADNIFFPDRPRTFDMHSLESSLIDIMRAE NDTIKGQSSSLFPMEDGFL
361	3	175	ERGAQVNATDEIKREIHHQLSIKPMAHSELVKSLP EDVSTYISKKTITETFPCLSV
362	58	1188	SEFKMLKRKPSNVSEKEKHQPKRSSSFQNFDRFRN NSLSKPDDSTEAHGDPNTNGSEQSKTSNNGGGLGK KMRAISWTMKKVGKKYIKALSEEKDEEDGENAHPY RNSDPVIGTHTEKVSLSKASDSMSLSYSGQSSSSGIT SCSDGTSNRDSFRLDDDGYPYSGPFCGRARVHTDFTP SPYDTSLSKIKKGDIIIDIICKTPMGMTGMLNNKVG NFKFIYVDVISEEEAAPKKIKANRRSNSKSKTLQE FLERIHLQEYTSLLLLNGYETLEDLKDIKESHLEL NIENPDDRRRLLSAAENFLEEIIQEQENEPEPLSL SSDISLNKSQLDDCPRDSGCYISSGNSDNGKEDLES ENLSDMVHKIIITEPSD
363	291	3	PAGRCPVSKGGAGLQAHNPAKTRTLLNETQIFS YFSQFGTVTQFRLSRSKMTGNGKGYAFVEFESEDA KIVAETMNNYLFGERLLECHGRV
364	3	574	SYLGDQSSEKLFDCSQCRKSFHCKSVLEHQRIHTQ EKPVKCTKCRKTRWRNSNFRHMRLEHEEKFYKQDE

			CREGFRQSPDCSQPGAPAVEKTFLLCQCGKTFTRK KTLVDHQRIHTGEKPYQCSDCGKDFAYRSAFIVHKK KHAMKRKPEGGPSFQSGHSVPGSSNSHKKKEPYKCS QCGKAFRNHS
365	3	608	SCNWFGKGRGFIMGIWNSHTSVGDILGSLIAGIWW NGQWGLSFIVPGIITAVMGVITFLFLIEHPEDVDCA PPQHHEGPAENQDNPEDPGNSPCSIKESGLETVAKC SKGPCEEPAAISFFGALRIPGVDEFSLCLLIAKLVS YTFLYWLPYIANVAHFSAKEAGDLSTLFHVGGIIG GIEAGLVSDYTNGRATTCCVM
366	1	636	LGKERKHLHQTKFADDFRKRHPNVHFLNQESMTLT GLPNHLAKAKQYVLKGGGMSSLAGKKLKEGHETPMD IDSDDSKAASPPLKGSVSSEASELDKKEKGICVICM DTISNKKVLPKCKHEFCAPCINKAMSYKPICTCQT SYGIQKGNQPEGSMVFTVSRDSLPGYESFGTIVITY SMKAGIQTEEHPNPGKRYPGIORTAYLPDNKE
367	3	2150	NKKTLEAPEGIRDKVSDEFLRQTLIGACSPFVPL LEGLRNGRNPLDLIAPGSRLECQAFQDSLSTWIVTV VENIGGRLKLRVEGLESSDNYEHWLYLDPFLHHVG WAAQQGYELQPPSAIRHLKNEAEWQEILAKVKEEEE EPLPSYLFKDKQVIGIHTFSVNMKLEAVDPWSPFGI SPATVVVKVFDEKYFLVEMDDLRPENHARRSFVCHAD SPGIFPVQWSLKNGLHISPPPGYPSQDFDWADYLKQ CGAEAAPQRCFPPLISEHEFKENMKLEAVNPILPEE VCVATITAVRGSYLWLQLEGSKKPIPECIVSVESMD IFPLGWCETNGHPLSTPRARVYKQKIAVVQPEKQ VPSSRTVHEGLRNQELNSTESVMINGKYCCPKIYFN HRCFSGPYLNKGRIAEPLQCVGPGNCVLVLRVLT LINAAYKPSRVLRRELQLDKDSVWHGCGEVLKAKYKG KSYRATVEIVKTADRVTEFCRQTCIK\LEC\CPNLF GPRMVLDKCSENCVLTCTKYTHYGGKKKNKRIGRP PG\GHSNLACALKKASKRRKRRKNVVFVK\KKRSSA SVDNTPAGFFPRGSGG*RMDDP\DEGDD\DSLSEG STSEQQDELQEESEMSEKKSCSSSPTQSEISTSLPP DRQRRKRELRTFSFSDDENKPPSPKEIDGQALLLT LPTVQECMDLKLGPAILCHHIERIKFAFYEQFAN

368	3	2150	<p>NKKTLEAPEGIRDKVSDDWDEFRLQTLTGACSPVPL  LEGLRNGRNPLDLIAPGSRLECQAFQDSLSTWIVTV  VENIGGRLKLYEGLESSDNYEHWLYYLDPFLLHVG  WAAQQGYELQPPSAIRHLKNEAEWQEIILAKVKEEEE  EPLPSYLFKDKQVIGIHTFSVNMKLEAVDPWSPFGI  SPATVVKVFDEKYFLVEMDDLRLPENHARRSFVCHAD  SPGIFPVQWSLKNGLHISPPPGYPSQDFDWADYLKQ  CGAAAPQRCFPPLISEHEFKENMKLEAVNPILPEE  VCVATITAVRGSYLWLQLEGSKKPIPECIVSVESMD  IFPLGWCETNGHPLSTPRRARVYQQRKIAVVQPEKQ  VPSSRTVHEGLRNQELNSTESVMINGKYCCPKIYFN  HRCFSGPYLNKGRIALPQCVGPGNCVLVLREVLT  LINAAYKPSRVLRRELQDKDSVWHGCGEVLKAKYKG  KSYRATVEIVKTADRVTEFCRQTCIK\LEC\CPNLF  GPRMVLKCSENC SVLT KTKYTHYYGKKKNKRIGRP  PG\GHSNLACALKKASKRRKRKNVVFVHK\KKRSSA  SVDNTPAGFFPRGSGG*RMDDP\DEGDD\DSLSEG  STSEQQDELQEESEMSEKKSCSSSPTQSEISTSLPP  DRQRRKRELRTFSFSDDENKPPSPKEIDGQALLLT  LPTVQECMDLKLGPAILKCHHIERIKFAFYEQFAN</p>
369	3	1285	<p>PGRMVSHTPAPPASFPVPLPGDPGAPCSSVLPTTG  ILTPHPGPQDSWKEAPAPRGNLQNRKNVNASFPTHSL  AHSPTMTF*FLGGFSQSFPFSDCPRPPPTYSSFLRT  LFFLFPSYTHTPVSSSLPSFPHSLFCLLVHCHSCHSP  KPEPWSLSG*THVFPSVSL\LPETFMPPAPITAPVM  SLTPELQGIPLPSQPPVSSSVHAPPGVPGELSLQVTR  TMYSPPLGNLPAALLGCRSW*MGLIPQGMG*GRLGAG  TRCPYCREREAAHLPSAVMGTV*L*VTGD*SLGKP  *EGQLAPLAFPLPASLSA\LQHLPEKMERKELPPEH  QSLKSSFEALLQRCSLSATDLKTKRKL EAAQORLEY  LYEKLCEGTLSPHVVAGLHEVARCVDAGSFEQGLAV  HAQVAGCSSFSEYSSFMPIKAVLIIAHKLIV</p>
370	2	3213	<p>TEADTCKNSPLDELEEGETRSDSETSKPQESFEKNS  KRRVSADVRKSKTIPRRGKSTVCLDKDSRKTHVRIH  QTNNKWNKRPDKSSRSSTEKKDKVMSTSSLEKIVP  IIAVPSSEQEIHMMLRMIRKHVRKNYMKFAKFSLI  QFHRIIESAILSFTSLIKHLNLHKISKSVTTLQKNL  CDIIESKCLKQVKNGIVDRLEQQLPDMKKKL\WKF  VDDQLDYLFAKLRKILVCDKSFGRDSDEGKLEKTS  KQNAQYSNRSEKGVWDNSNRGIAGKEKLSKIRKDPV  HYK/SL*VGGVKKSEENYQDQNNSSINTVKHDIKKN  FNICFDNIKNSQSEERSLEVHCPSTPKSEKNEGSSI  EDAQTSQHATLKPERSONFEILTEQQASSLTFLNLSDA  QMGEIFKSLQGSDDLNSNVNCTEKSEWELKTPEKQ  LLETLCESIPACTTEELVSGVASPCPKMISDDNWS  LLSSEKGPLSSGLSLPVHPDVLDSCMFVSTNLP  LSKDNVCSVEKSKPCVSSILLED LAVSLTVPSPLKS  DGLHSFLKPDMSSSSTPEEVISAHFSEDALLEGRGI  AFLARYFILALESDNSSKSSSS\WTSRS\VAPG  FQYHPNLPMAVIMEKSNDFIVKIRRATPSTSSGL  KQSMMPDELLTSLPRHGKEADEGPEKEYISCQNTVF  KSVBELENSNKNVDGSKSTHEEQSSMIQTQVPDIYE  FLKDASDKMGHSDEVADECFLKHQVWETKVPESIEE  LPSMEEISHSVGEHLNPTYVDLTKDPVTETKNLGEF  IEVTVLHIDQLGCSGNLNQSAQILDNSLQADTVGA  FIDLTQDASSEAKSEGNHPALAVEDLGCGVIQVDED  NCKEEKAQVANRPLKCIVEETYIDLTTESPSSCEVK</p>

			KDELKSEPGSNCNSELPGTLHNSHKRRNISDLNH PHKKQKQKETDLTNKEKTKKPTQDSCENTEAHQKKAS KKKAPPVTKDPSSLKATPGIKDSSAALATSTSLSAK NVIKKKGEEIILWTRNDDREILLECQKRGPSFKTFA YLAAKLDKNPNQVSERFQQLMKLFEKSKCR
371	7	1361	PALLEFRTRLMDLGQLRGVPAYRVHV*RVGSLLTGD AFTHV*LG/GKDRKIYCTDLRNPDIRVLICEEKAPV LKMELDRSADPPPAIWVATTSTVKNWTLKGIHNR ASGDYDNDCTNPITPLCTQPDQVIKGGASIIQCHIL NDRRHILTKDTNNNVAYWDVLKACKVEDLGKVD FED EIKKRFRKMVYVPNWFSVDLKTGMLTTITLDESDFAA WWSAKDAGFSSPDGSDPKLNLGGLLQALLEYWPR HVNPMDEEENEVNHVNGEQENRVQKNGYFQVP PHT PVI FGEAGGRTLFRLLCRDSGGETESMLLNETVPQW VIDITVDKNMPKENKIPFYLQPHASSGAKTLKKDRL SASDMLQVRKVMHVYKI INLDNESQTTSSSNNEK PGEQKEEDIAVLAEEKIELLCQDQVLDPNMDLRTV KHF IWKSGGDLTLHYRQKST
372	1	92	FKKSNKF*YKRCN*KSSMCRSSSRDLGAE*IINEL KRQKTMHTEAQRDKQMENTEKSIRDLDWRVSRPNML LLEVSEENKENGIEAIFEEIMAVNFPKL*KTSSHR LKHYEPQTGEIQRYKQL\R*KRRIIFSGATAWLTA DF*TKAMESR*QWNE/QCRKEYPSK/SEGELKMFSD KKNMRKYIASRLALKEILNGII*AE
373	2	3246	ENAVGSWTDDLTLQSLSLKDTLSAYISADDISILNER VELLQWHEELCHQLSLRRQIGERLNEWAVFSEKN KELCEWLTQMESKVSQNGDILIEEMIEKLKDYQEE IAIAQENKIQLQOMGERLAKASHESKASEIEYKLGK VNDRWQHLLDLIAARVKKLKETLVAVQQLDKNMSSL RTWLAHIESELAKPIVYDSCNSEEIQKRLNEQQELQ RDIEKHSTGVASVLNLCEVLLHDCDACATDAECD SI QQATRNLD RRWRNICAMSMERRLKIEETWRLWQKFL DDYSR\FEDWLKSSERTAAFSSSGVIYTVAKEELK KFEAFQRQVHECLTQLELINKQYRRLARENRTDSAC SLKQMVHEGNQRWDNLQKRVTSILRRLKHFIGQREE FETARDSILVWLTEMDLQLTNIHFSECDVQAKIKQ LKAFQOEISLHNHKEBQIIAQGEQLIEKSEPLDAAI IEEELDELRRYCQEA FGRVERYHKKLIRLPLPDDEH DLSRELELED SAALS DLHWHDRSADSLLSPQPSSN LSLSLAQPLRSERSGRDTPASVDSIPLEWDH DYLS RDLESAMSRALPSEDEEGQDDKDFYLRGAVGLSGDH SALESQIRQLGKALDDSRFQIQQTENIIRSKTPTGP ELDTSYKGYMKLLGECSSSIDSVKRLKHLKEEES LPGFVN LHSTETQTAGVIDRWELLQAQALSKELRMK QNLQWQQFNSDLNSI WAWLGDTEEELEQLQRLELS TDIQTIELQIKKLKELQKAVDHRKAILLSINLCSPE FTQADSKE SRDLQDRLSQMNGRWDRCVSLLEEW RGL LQDALMQCQGFHEM SHGLLLMLNIDRRKNEIVPID SNLDAEILQDHHKQLMQIKHELLESQLRVASLQDMS CQLLVNAEGTDCLEAKEKVHVIGNRLKLLKEVSRH IKELEKLLDVSSSQDLSSWSSADELDTSGSVSPTS GRSTPNRQKTPRGKCSLSQPGPSVSSPHSRSTKGG DSSLSEPGPGRSGRGMFRVLRAALPLQLLLLLLIG LACLVP MSEEDYSCALSNNFARSFHPMLRYTNGPPP L

374	1	2430	MNAVGSPEGQELHKLGSRAWNDNPAYSGPPSPHGTLR VCTISSTGPIQPQPKPEDEPQETAYRTQVSSCCLH ICQGIRGLWGTTLTENTAENRELYIKTTLRELLVYI VFLVDICLLTYGMTSSSAYYTKVMSEFLHTPSDT GVSFQAISSMADFWDFAGQPLDLSLYWTKWYNNQSL GHGSHSFIYYENMLLGVPRRLQKVRNDS CVVHEDF REDILSCYDVYSPDKEEQLPFGPFNGTAWTYHSQDE LGGFSHWGRLTSYSGGGYLDLPGSRQGSAAELRAL QEGWLDRGTRVVFIDFSVYNANINLFCVLRVVEF PA\TGGAIPSWQIRTVKLIRYVSNDFFIVGCEVIF CVFIFYVVEEILELHHRRLRYLSSIWNILDVLVIL LSIVAVGFHIFRTLEVNRLMGKLLQOPNTYADFEFL AFWQTQYNNMNAVNLFFAWIKIFYISFNKMTMTQLS STLARCAKDILGFVMMFVFFAYAQGLYLLFGTQV ENFSTFIKCIFTQFRIILGDFDYNAIDNANRILGPC PTLSPYVFFVFFVLL\NMFL\AIIND/TQYSEVKEE LAGQ\KDELQSDLLKQGYNKTLRLRLRKERVSDV QKVLQGGQEIQFEDFT\NTLRELGHAEHEITELTA TFTKFDNRDGNRILDEKEQEKMRQDLEEEVALNTEI EKLGRSIVSSPQKSGPEAARAGGWVS GEEFYMLTR RVLQLETVLEGVVSQIDAVGSKLMLERKGLAPSP GVKEQAIWKHPQAPAVTPDPWG\VOGGQSESEVPYK REEEALEERLSRGEIPTLQRS
375	2313	1475	DDGAHVMMHREVWMAVFSYLSHQDLVCVMRVCRTWN RWCCDKRLWTRIDLNHCKSITPLMLSGIIRRPVSL DLSWTNISKQLSWLINRLPGLRDLVLSGCWSLAVS ALCSSSCPLLRLTLDVQWVEGLKDAQMRDLSPTDN RPGQMDNRSKLRNIVELRLAGLDITDASRLRIIRHM PLLSKLHLSYCNHVTQDSINLLTAVGTTTRDSLTEI NLSDCNKVTQCLSFFKRCGNICHIDLRYCKQVTKE GCEQFIAEMSVSVQFGQV\EEKLLQKLS
376	1157	481	SWPGQAEPSEREFVVRERAAETRGSEVFEIMNPVYSP GSSGVPPYANAKGIGYPAGFPMGYAAAAPAYSPNMYP GANPTFQTYTPGTPYKVSCTSGAVPPYSSSPNP YQTAVYPVRSAYPQQSPYAQQGYTQPLYAAPPHV IHHTTVVQPNGMPATVYPAPIPPPRGNGVTMGMVAG TMAMSAGTLLTAHSPTPVAPHPVTVPYTYRA\QGTP TYSYVPPQW
377	1	212	VTAIIDGTGSIGTALGPLLAGLISP\TGWNNVFYML ISADVLACLLLCRLVYKEILAWKVSLSRSGSYKEI
378	237	1276	NSSALKGLVMVKAATDSRKGMAFCSVT*PCCSTLQE VLNHSDDHPILFLSNLVEGTYTFFHLKVTDAKESDT DRTTVEVKPDPRKNNLVEIILDINVSQTERLKGMF IRQIGVLLGVLDSDIIVQKIQPYTEQSTKMVFFVQN EPPHQIFKGHEVAAMLKSELRKQKADFLIFRALEVN TVTCQLNCSDHGHCDSTFKRCICDPFWMENFIKVQL RDGDSNCEWSVLYVIIATFVIVVALGILSWTVICCC KRQKGKPKRKSKYKILDATDQESLELKPTS RAGIKQ KGLLLSSSLMHSESELDSDDAIFTWPDREKGLLHG QNGSVPNGQTPLKARS PREIL



379	3	850	<p>             IIEKLAEGLDIQLKSPVQCIDYPGDEVQVTTTDTGTG              YSAQKVLVTPLALLQKGAIQFNPLSEKKMKAINS              LGAGIIEKIALQFPYRFWDSKVQGADFFGHVPPSAS              KRGLFAVFYDMDPQKKHSLMSVIAGEAVASVRTLD              DKQVLQOCMATLRGLFKEQEVDPDTKYFVTRWSTDP              WIQMAYSFVKTGGSGEAYDIIAEDIQGTVFVAGEAT              NRHFPQTVTGAYLSGVREASKIAAF*EFGGPSFLLY              PRWGNLNLHMLNLSFIRGKNRLYIVKLKCF           </p>
380	28	349	<p>             EYRRLEQG*PNDIYILYPKTVEGTSFSPAPGTLTKT              DH/IAGSRNMQNMFSHDN*SEK*ITKI*HKEPPYIQ              KLNFTLLNNSRVKBEITREIRKYLGLNDKN\Y*NVWD              A           </p>
381	1	1407	<p>             LQQTEDKSLNQGSSSEEVAGSSQKMGQPGPSGSDS              LATALHRLSLRRQNYLSEKQFFAEWQRKIQVLADQ              KEGVSGCVTPTESLASLCTTQSEITDLSSASCLRGF              MPEKLQIVKPLEGSQTLYHWQQLAQPNLGTILDPRP              GVITKGFTQLPGDAIYHISDLEEDDEEGITFQVQQP              LEVEEKLSTSKPVTGIFLPPITSAGGPVTVATANPG              KCLSTCNSTFTTTCRILHPSDITQVTPSSGFPPLS              CGSSGSSSNTAVNSPALAYRLSIGESITNRRDSTT              TFGSTMSLAKLLQERGISAQVYHSPISENPLQPLPK              SLAIPSTPPNSPSHSPCPSPLPFEPVHLSENFLAS              RPAETFLQEMYGLRPSRNPPDVGQLKMNLDRLKRL              GIARVVKNPGAQENGRCQAEIGPQKPD SAVYLN SG              SLLGGLRRNQSLPVMGSAAPVCTSSPKMGVLKE              D           </p>
382	2104	96	<p>             SSGAPAAGAAPAMGEEDYYLELCERPVOFEKANPVN              CVFFDEANKQVFAVRSGGATGVVVKGPDNRNPI SFR              MDDKGEVKCIKFSLENKILAVORTSKTVDFCNFIPD              NSQLEYTQECKTKNANILGFCWTSSTEIVFITDQGI              EFYQVLPEKRSKLLKSHNLNVNWMYCPESAVILL              STTVLENVLQPFHFRAGTMSKLPKFEIELPAAPKST              KPSLSERDIAMATIYGQLYVFLRHHRSRTSNSTGAE              VVLYHLPREGACKMHILKLNRTGKFALNVVDNLVV              VHHQDTETSVIFDIKLRGEFDGSVTFHHPVLPARSI              QPYQIPITGPAAVTSQSPVPCKLYSSSWIVFQPDII              ISASQGYLWNLQVKLEPIVNLLPDKGRLMDFLQRK              ECKMVILSVCSQMLSESDRASLPVIATVFDKLNHEY              KKYLDAEQSYAMAVEAGQSRSSPLLKRVPVRTQAVLD              QSDVYTHVLSAFVEKKEMPHKFVIAVLMHEYIRSLNQ              FQIAVQHYLHELVIKTLVQHNLFYMLHQFLQYHVLS              DSKPLACLLLSLESFYPPAHQLSLDMLKRLSTANDE              IVEVLLSKHQVLAALRFIRGIGGHDNISARKFLDAA              KQTEDNMLFYTIFRFFEQRNQRRLRGSPNFTTGEHCE              EHVAFFKQIFGDQALMRPTTF           </p>
383	63	1094	<p>             TLNYP AENSFNHRPYTACDFIEGIYRTERDKGTYE              LTFKGDHKHEFKRLILFRPFGPIMKVKNKLNLMANT              LINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLT              VVYFGKEEINEVKGILENTSKAANFRNFTFIQLNGE              FSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLN              TCRLNTQPGKKVFYPVLF SQYNPGIIYGHHDVAPP              EQQLVIKKEGTGFWRDFGFGMTQCYRSDFINIGGFDL              DIKGWGGEDVHLYRKYLHSNLIVRTPVRGLFHLWH              EKRCMDLTPEQYKCMQSKAMNEASHGQLGMLVFR              HEIEAHLRKQKQKTSSKKT           </p>

384	792	494	FLKVEISIQSNFQPGMKLEVANKNNPDYVWATIT TCGQLLLRLRYCGYGEDRRADFWCDVVIADLHPVGWC TQNNKVLMPDPGEPLFQRLRFTSRHPS
385	148	428	SLGWGLDILQLLDLFIQWDWSTYLADYGQPNCKYLR VNPVTALTLEKISREMKDTSRKNNMFAQFRKNERD KQKLIDSVAKQLRGLISSHS
386	1052	602	GQDDTSKADKPKVDEEGDENEDDKDYHRSDPQIAIC LDCLRNNQSGDINVVKGLMKFIRCSTRVTGTIKK FLSLKLKLPSSYELDVLCNGEIMGKDHTMEFIYMTR WRLRGENFRCLNCSASQVCSQDGPPLYQSYPMVLQYR PRIDFG
387	2	2175	GEKGGMKPPAHWTGGLQPELQGSPPAGWDSTEGWTWG DGEHGLGAAAMPTWGARPASPDRFAVSAEANKVRE QQPHVBRIFSVGVSVLPKDCPDNPHIWLQLEGPKEN ASRAKEYLKGCLSPQLQDEIHYPKHLHCIFLGAQGF FLDCLAWSTSAHLVPRAPGSLMISGLTEAFVMAQSR VEELAERLSWDFTPGPSSGASQCTGVLRDFSALLQS PGDAHREALLQLPLAVQEEELSLVQEASSQGPGAL ASWEGRSSALLGAQCQGVRRAPPSDGRESLDTGSMGP GDCRGARGDTYAVEKEGGTQGGPREMDLGWKEPGE EAWEREVALRPQSVGGGARESAPLKKGALGKEEIAL GGGGFCVHREPPGAHGSCHRAAQSRSASLLQRLHNG NASPPRVPSPPPAPEPPWHCGDRGDCGDRGDVGDGRG DKQQGMARGRGPPQWKRGARGGNLVTGTQRFKEALQD PFTLCLANVPGQPDLRHIVIDGNSVAMVHGLQHYFS SRGIAIAVQYFWRGRHRDITVFPQWRFSKDAKVR SHFLQKLYSLSLSLTPSRVMDGKRISYDDRFMVK LAEETDGIIVSNDQFRDLAESEKWMAIIRERLLPF TFVGNLFMVPPDDPLGRNGPTLDEFLKKPARTQGS AQHPSRGFAEHGKQQQGREEEKSGGIRKTRERERL RRQLLEVFQWQDHKVDLQREPYCRDINQLSEALL SLNF
388	2059	720	IDTGSYVVAQAGVKLLGSSSYPTSASQSALITGLSH RAWPRYISLLTSHRYENGRGSSHQQVTCYPFKDVN NWWIVKDPRRHQLVSSPPRPVRHGMVQLVHGMMT RSLNTHDVAAPLSPHSQEVSCYIDYNISMPAQNLR LEIVNRGSDTDVWKTILSEVRFVHVNTSAVLKLSGA HLPDWGYRQLEIVGEKLSRGYHGSTVWNVVEHRYGA SQEQREERELHSPAQVDVSRNLSFMARFSELOWRM LALRSDDSEHKYSSSPLEWVTLDTNIAWLHPRTSA QIHLGNIVIVWSGSLALAIYALLSLWYLLRRRRNV HDLPPQDAWLRLWLAGALCAGGAVNYLPFFLMEKTL FLYHYLPALTFFQILLPVVLQHISDHLCSQLQRSI FSALVVAWYSSACHVSNTLRPLTYGDKSLSPHELKA LRWKDSWDILIRKH
389	1	1782	ETDNDLTKEYEGKENVSFELQRDFSQETDFSEASL LEKQQEVHSAGNIKKEKSNTIDGTVKDETSVVEECF FSQSSNSYQCHTITGEQPSGCTGLGKSISFDTKLVK HEIINSEERPFCCEELVEPFRCDSQLIQHQENNT KPYQCSECGKAFSINEKLIWHQRLHSGEKPFCVEC GKSFSYSSHYITHQTIHSGEKPQCKMCGKAFSVNG SLSRHQRIHTGEKPYQCKECCNGFSCSSAYITHQRV HTGEKPYECNDCGKAFNGNAKLIHQRIHTGEKPYE CNECGKGFRCSSQLRQHQSHTGEKPYQCKECCGKGF NNNTKLIHQRIHTGEKPYECTECGKAFSVKGLIQ HQRIHTGEKPYECNECGKAFRCNSQFRQHLRIHTGE

			KPYECNECGKAFSVNGKLMRHQRIHTGEKPFECNEC GRCFTSKRNLLDHHRIHTGEKPYQCKEKGKAFSINA KLTRHQRIHTGEKPFKCMCEKAFSCSSNYIVHQRI HTGEKPFQCKEKGKAFHVNAHLIRHQRSHTGEKPF CVECCKGFSFSSDYIIHQTVHTWKKPYMCSVCGKAF RFSFQLSQHQSVHSEKGS
390	2	1419	VRTPYDLNITYLEEVDVVAEYELEYLLLEGHCYD ITTGQPPRGLQFTLGTSANPVIIVDTIVMANLGYFQL KANPGAWILRLRKRSEDIYRIYSHDGTDSPPDADE VVIVLNNFKSKIIKVKVQKKADMVNEDLLSDGTSEN ESGFWDSEFKWGTGQKTEEVKQDKDDIINIFSVASG HLYERFLRIMMLSVLKNTKTPVKFWFLKNYLSPTFK EFIPYMANEYNFYELVQYKWPRLHQOTEKQRIIW GYKILFLDVLFLVVDKFLVDADQIVRTDLKELRD FNLDGAPYGYTPFCDSRREMDGYRFWKSGYWASHLA GRKYHISALYVVDLKKFRKIAAGDRLRGQYQGLSQD PNSLSNLDQDLNNMIHQVPIKSLPQEWLWCETWCD DASKKRAKTIDLCNNPMTKEPKLEAAVRIVPEWQDY DQEIQLQIRFQKEKETGALCQREAQKNPSRKGPQK REEL
391	1	610	RCAVLFCSSCSKVIQVGVHGGMLGIIQRAMVKACP HVWFERSEMKDRHLVTKRLKEHIADKKLPILIFPE GTCINNTSVMMFKKGSFEIGGTIHPVAIKYNPQFGD AFWNSSKYNMVSYLLRMMTSAIVCDVWYMPMTRE EGEDAVQFANRVKSAIAIQGGLTELPWDGGLKRAKV KDIFKEEQKNYSKMIVGNGSL
392	1	4913	QLRGESDRSKQPPPASSPTKRKGRSRALEAVPAPPA SGPRAPAKESPCKRVPDPSVTKGTAAESGEEAARA IPRELVPKSSSLPEIKPEHKRGPLPNHFNRAEGG RSRELGRAAGAPGASDADGLKPRNHFGVGRSTVTTK VTLPAKPKHVELNLKTPKNLDSLGNENPFSPVHK GNTATKISLFEKRTNSSPRHTDIRGPRNTPASSKT FVGRAKLNLAKKAKEMEQQEKKVMPNSPQNGVLVKE TAIETKVTVSEEEILPATRGMNGDSSSENQALGPQPN QDDKADVQTDAGCLSEPVASALIPVKDHKLEKEDS EAADSKSLVLENTDTAQDIPPTVDTKDLPTAMPK PQHTFSDSQSPAESSPGPSLSLSAPAPGDVPKDTCV QSPISFPCTDLKVSSENHKGCVLPVSRQNEKMPLL ELGGETTPPLSTERSPEAVGSECPSRVLVQVRSFVL PVESTQDVSSQVIPESSEVREVQLPTCHSNEPEVVS VASCAPPQEEVLGNEHSHCTAELAAGSGPQVIPPAS EKTLPQAQSQSGSRTPLMAESSPTNSPSSGNHLATP QRPDQTVTNGQDSPASLLNISAGSDDSVFSSSDME KFTEI IKQMSAVCMMPKRRKARMPNSPAPHFAMPP IHEDHLEKVFDPKVFTFGLGKKKESQPEMSPALHLM QNLDTKSKLRPKRASAEQSVLFKSLHTNTNGNSEPL VMPEINDKENRDVTNGGIKRSLEKSALFSSLLSSL PQDKIFSPSVTSVNTMTTAFSTSQNGSLSQSSVSQP TTEGAPPCGLNKEQSNLLPDNSLKVFNFNSSSTSHS SLKSPSHMEKYPQKEKTKEDLDSRNLHLPETKFSE LSKLNDDMEKANHIESVIKSNLPNCANSDDTFMGL FKSSRYDPSISFSGMSLSDTMTLRGVSQNKLNPRPG KVVIYSEPDVSEKCEVFSDIQDCSSWSLSPVILIK VVRGCWILYEQPNFEGHSIPLEEGELELSGLWGIED ILERHEEAESDKPVVIGSIRHVVDYRVSHIDLfte PEGLGILSSYFDDTEEMQGFVGMQKTCMKVHWGTW

			LIYEEPGFQGVPPFILEPGEYPDLSFWDTEAAYIGSM RPLKMGGKVEFPTDPKVVVYEKPFEGKCVELETG MCSFVMEGGETEEATGDDHLPFTSVGSMKVLRGIVW AYEKPFGTGHQYLLLEEGEYRDWKAAGGYNGELQSLR PILGDFSNAHMIMYSEKNFGSKGSSIDVLGIVANLK ETGYGVKTQSINVLSGVWVAYENPDTGGEQYILDKG FYTSFEDWGGKNYKISSVQPICLDSFTGPERRNQIH LFSEPPQFGHSQSFEETTSQIDDSFSTKSCRVSOGS WVVDGENFTGNQYVLEEGHYPCLSAMGCPPGATFK SLRFIDVEFSEPTIILFEREDFKGKKIELNAETVNL RSLGFNTQIRSVQVIGGIWVTYEGSYRGRQFLLSP AEVPNWYEFSGCRQIGSLRPFVQKRIYFRLRNKATG LFMSTNGNLEDLKLRLRIQVMEDVGADDQIWIYQEGC IKCRIAEDCCLTIVGSLVTSKSLGLALDQONADSQF WSLSDGRIYSKLPNLVLDIKGGTQYDQNHIIILNT VSKEKFTQVWEAMVLYT
393	1978	1670	LFIGGPSNMIRSAISADLGRQELIQRSSEALATVTG IVDGSIGSIGAAVGQYLVSILRDKLGMWVVFYFILM TSCITVFISPLIVREIFSLVLRRAHILRE
394	110	1220	RRQLGVALIPSHRMDYKSSLIQDGNPMENLEKQLIC PICLEMFTKPVVILPCQHNLCRKCANDIFQAANPYW TSRGSSVSMGGRFRCPTCRHEVIMDRHGVYGLQRN LLVENIIDIYKQECSSRPLQKGSHPMCKEHEDEKIN IYCLTCEVPTCSMCKVFGIHKACEVAPLQSVFQGGK TELNNCISMLVAGNDRVQTITQLEDSSRRVTKENSH QVKEELSQKFDLYAILDEKKSELLQRITQEKEKLL SFIEALIQQYQEQOLDKSTKLIVETAIQSLDEPGGATF LLTAKQLIKSIVEASKGCQLGKTEQGFENMDFFTLT LEHIADALRAIDFGTDEEEEFIEEDQEEESTEG KEEGHQLGAG
395	3	695	VKTHFTCKDA*RLKVK**NIFHANEKQKQARVAIV VSGKIDFKNGKN\KNNNEDDHYIMTKR*IQQEDIPV LNIYAYA/STGAQRYIKEILFDLKGEDSNTIMVGD L/NPLSASDRSCRQKIN\MD*NCALDQIGLTDIYRT FYLTAGECTFFLSAHVTFSRIDHVLGHKTSLNKILK IEIISSIFLDHKG/IKLEFNKNFNGSCTNTWKVVK MLMTNYWVSEEIMKEIKKKK
396	1139	544	YGCEKTTEGTDGVNFYNILTKSTPTSTMESSLEFTQ SHLVCLCQRHVRHLQDALSQLMNGPIRKKLKIIE DQSWGQATNVFVNMEEDFMKPVISIVDELLEAGIN VTVYNGQLDLIVDTMGQEAWRKLKWPPLPKFSQLK WKALYSDPKSLETSAFVKS YKNLAFYWLKAGHMVP SDQGDMAKMMRLVTQOE
397	3	574	GSTHASANICEVCNKWGRLFCCDTCPRSFHEHCHIP SVEANKNPWSCIFCRIKTIQERCPEQSQGHQSEVL MRQMLPEEQKCEFLLLKVYCDKSCFFASEPYYNR EGSQGPQKPMWLNKVKTSLEQMYTRVEGFVQDMRL IFHNHKEFYREDKFTRLGIQVQDIFEKNFRNIFAQ ETSKNIIMFI
398	2	523	FVPCKLLIPERDPLEEIAESSPQTAANSAAELLKQG AACNVWYLSNVEMESLTGHQAIQKALSITLVQEP VSTVVFVKVSAQGITLTDNQRKLFRRHYPVNSVIF CALDPQDRKWIKDGPSSKVFGFVARKQGSATDNVCH LFAEHDEQPASAIVNFVSKVMIGSPKKV

399	2769	1120	AFSVFFVCVAFSTSNIIICLLFIPIQWLFFAASTYVWV QYVWHTERGVCCLPTVSLWILFVYIEAAIRFKDLKNF HVDLCRPFAAHCIGYPVVTLGFGFKSYVSYKMRLRK QKEVQKENEFYMQLLQOALPPEQOMLQKQEKEAEEA AKGLPDMSSILIHNGGIPANKKLSSTLPEIEYRE KGKEKDKDAKHNLGINNNNILQPVDSKIQEIEYME NHINSKRLNNDLVGSTENLLKEDSCTASSKNYKNAS GVVNSSPRSHSATNGSIPSSSSKNEKKQKCTSKSPS THKDLMECIPNNQLSKPDALVRLEQDIKKLKADLQ ASRQVEQELRSQISSLSSTERGIRSEMQLRQENEL LQNKLNNAVQMKQDKQNISQLEKKLKAQEARSFV EKQLMEEKKRKKLEEATAARAVAFAAASRGECTETL RNRIRELEAEGKKLTMDMKVKEDQIRELELKVQELR KYKENEKDTVLMSALSAMQDKTQHLENSLSAETRI KLDLFSALGDAKRQLEIAQGQILQKDQEIKDLKQKI AEVMGRHAQP
400	3	1470	IRISRVDDFVKLIRLSQIKEKMAREKLEEIDWVTFG VILKKVTPQSVNSGKTFSIWKLNLDRLTQCVSLFL FGEVHKALWKTEQGTVVGILNANPMKPKDGSEEVCL SIDHPQKVLIMGEALDLGTCKAKKNGEPTQTQTVNL RDCEYCQYHVQAQYKKLSAKRADLQSTFSGGRIPKK FARRGTSCLKERLCQDGFYGGVSSASYAASIAAAVA PKKKIQTTLNVLVKGNTLIIQETROKLGIPOKSL CSEEFKELMDLPTCGARNLKQHLAKATASGIMGSPK PAIKSISASALLKQKQRMLEMRRRKSEIQRFLQ SSSEVESPAVPSSSRQPPAQPPRTGSEFFRLEGAPA TMTPKLGRGVLEGDDVLFYDESPPPRPKLSALAEAK KLAAITKLRAKGQVLTKTNPNSIKKKQKDPQDILEV KERVEKNTMFSSQAEDELEPARKKRREQLAYLEFEE FQKILKAKSKHTGHPERGRG
401	989	370	FLQMRQHRDPHILQKPFNVTETRCCLKPSRTTSWCK AIPPDSEKSIICDNLSELMMAMQDELDQMSMEHQE LLKQMKETESHVCDDECELECLLKIMEIKGEQIS KLKKHQDSVCKLQKQVQNSKMSEASGIQEDSYPKG SKNIKNSPRKCLTDNLQKNSSFHPIRVHNLQMKL RRDDIMWEPVTKQONCHLNLGLWSVRP
402	3	568	RPGFPWQEIPIKVSGLSLSLVSQHMK* KSVQLLFR L/RGDIATEQVDVINSTARTFNKSGVSRAILEGA QAVESECAVLAAQPHRDFIITPGGLCKKIIHVP GGKDVKRTVTSVLEECQQRKYTSVSLPAIGTGNAGK NPITVADNIIIDAIVDFSSQHSSTPSLKTVKVVFQPE LLNIFYDSM
403	384	16	WELLTAIWTPLCGFSSSWKGSMLDRCEAPVHPEKC PPDLRAGMIALSPVSLYISAWFSFLFSVPRFIVLCR FVLSPCRPHLFIFV*QILLEAY*IPFTVIGQGTWW* AGQNSCPHTKSSTRE
404	3	1285	KLAEASYKETQMVKIKEEPMEDIQDSHVSISPSRN VGYSTLIGREKTEPLQKMEGRVPPERNLFSQDISV KMAELLFQLSEKVSKEHNHTKENTIRTTTSPFFSE DTFRQSPFTSNSKELLPSDSVLHGRISAPETEKIVL EAGNGLPSWKFNQDLFPDVCVGKVFGRQOTLSRHLS LHTEERKYKCHLCFYAAKCRANLNQHLTVH/CREAG EYRHRGHCQRRHL*R\HDGKKHPYYSCHVCGFETE LNVQFVSHMSLHVDKEQWMFSCCTACDFVTMEEEAE IKTHIGTKHTGEDRKTPSESNSPSSSSLSA\RVIQ TAKMIQMAPRKTRAGTICWSSLSCL/VSQPSLNSEE

			KPEKGFECVFCNFVCKTKNMFERHLQIHLITRMFEC DVCHKFMKTPEQLLEHKKCHTVPTGGNLNCSRMTK
405	106	309	RQCLTLLPRLECGGMIRTDNLELMGSSDPPALASQ NPGI\TDVSHHTGQILTSLLLKYKCLICRHIF
406	3	1760	AASRTMGSRHFEGYIDHVGHFGRFQRVLYFICAFQ NISCGLHYLASVFMGVTPHHVCRPPGNVSQVVFHNH SNWSLEDTGALLSSGQKDYVTVQLQNGEIWELSRCS RNKRENTSSLGYEYTGSKKEFPDVGYYIDQNTWKS TAVTQWNLVCDRKWLAMLIQPLFMFGVLLGSVTFGY FSDRLGRRVVLWATSSSMFLFGIAAAFAVDYYTFMA ARFFLAMVASGYLVVGFVYVMEFIGMKSRTWASVHL HSFFAVGTLLVALTGYLVRTWWLYQMILSTVTVPFI LCCWVLPETPPFWLLSEGRYEEAQK\IVDIMAKWNR SSCKLSELLSLDLQGPVSNSTEVQKHNLSYLFYNW SITKRTLTVWLIWFTGSLGFYSFSLNSVNLGGNEYL NLFLLGVEIPAYTFVCIAMDKVGRRTVLAYSFLC\ SALACGVVMVIPQKHYILGVVTAM\VGKILPIGA AFG\LIYLYTAELYPTIVRSLAVGSGSMVCRLASILAP FSVDLSSIWIFIPQLFVGTALLSGVLTILKLPETLG KRLATTWEEAAKLESENESSKSKLLLTNNSGLEKT EAITPRDSGLGE
407	3	2944	HLLHRWFQTDQMNFITTTGEFQLTEACPYLGTTHSEE SRFGILHLHLQPLEMKRVGVFTPADYGVKVTSLILI RNNLTVIDMIGVEGFGARELLKVGGRPLPGAGGSLRF KVPESTLMDCRRQLKDSKQILSITKNFKVENIGPLP ITVSSSLKINGYNCQGYGFVLDCHQFSLDPNTSRDI SIVFTPDFTSSWVIRDLSLVTAADLEFRFTLNVTLP HLLPLCADVVPGPSWEESFWRLTVFFVSLSLGVI LIAFQQAQYILMEFMKTRQRQNASSSSQNNGPM DVISPHSYKSNCKNFLDTYGPSDKGRGKNCLEPVNT PQSRIONAAKRSPATYGHSSQKKHKCSVYYSKHKT STAAASSTSTTTEEKQTSPLGSSLPAAKEDICTDAM RENWISLRYASGINVNLQKNLTLPKNLLNKEENTL KNTIVFSNPSSSECSMKEGIQTCMFPKETDIKTSE NTAEFKERELCPLKTSKKLPENHLPRNSPQYHQP DLPEISRKNNGNNQQVPVKNVDHCENLKKVDTKPS SEKKIHKTSREDMFSEKQDIPFVEQEDPYRKKKLQ EKREGNLQNLNWSKSRTCRRKKNRGVAPVSRPPEQ SDKLVCSDFERSELSSDINVRSWCIQESTREVCKA DAEIASSLPAAQREAEQYQKPEKKCVDFCSDSSD CGSSSGSVRASRGWSGSWSSTSSSDGDKKPMVDA QHFLPAGDSVSQNDFPSEAPISLNLSHNICNPM TGNSLPQYAEPSCPSLPAGPTGVEEDKGLYSPG DLWPTPPVCVTSSLNCTLENGVPCVQIESAPVH NSFIDWSATCEGQFSSAYCPLELNDYNAPPEEN MNYANGFPCPADVQTDFFIDHNSQSTWNTPP\N MPAS\WGNAQFPSSSRPYLKSTPKACLPM SGLFGPI\WAP\QSDVYENCCPINPTTEHSD/ THMENQA\VVCKEYYPGF\NPFPRAYMNLDIW TTTT\ANRNA NFPLSRDSSYCGNV
408	5	2330	NPILWLETOMASNERDAISWYQKKIGAYDQQIWEKS IEQTQIKGLKNKPKMGHIKPDLDVLDLIRGSTFAK AKPEIPWTSLTRKGLVRVVFPLFSNWWIQVTS LRI FVWLLLLLYFMQVIAIVLYLMMPIVNI SEVLGPLCLMLLMGTVHCQIVSTQITRPSGNN GNRRRRKLRTVNGDGSRENGNNSDKVRGIET LESVP IIGGFWETIFGNRIKRVKLISNKG TETDNDPSCVHPIIKRRQCRPEIR

			<p>MWQTREKAKFSDGEKCRREAFRRLLGNGVSDDLSSSEE  DGEARTQMILLRRSVEGASSDNGCEVKNRKSILSRH  LNSQVKKTTTRWCHIVRDSDSLAESEFESAAFSQGS  RSGVSGGSRSLNMSRRDSESTRHDSETEEDMLWDDLL  HGPECRSSVTSDSEGAHVNTLHSGTKRDPKEDVFQQ  NHLFWLQNSSPSSDRVSAIIEWEGNECKMDMSVLEI  SGIIMSRVNAYQQGVGYQMLGNVVTIGLAFFPFLHR  LFREKSLDQLKSISAEIILTLFCGAPPVTPPIIVLSI  INFFERLCLTWMFFMMCV\AERTYK\QRFLPAKLF  SHIYFCQGKLGKYEIPHFRLKKVENIKIWLSLRSYL  KRRGPQRSVDV\VSSVFLTLTSLAFICCAQVLQ\G  HKT\SWNDAY\NWGVFDLGETALLFLRLASLGSE  TNKKYSNVSIILLTEQINLYLKMEKKPNKKEQLTLVN  NVLKLSTKLLKELDTPFRLYGLTMNPLIYNITRVVI  LSAVSGVISDLLGFNIRLWKIKS</p>
409	3963	827	<p>LSRSSSDNNTNTLGRNVMSTATSPLMGAQSFNLT  PGTSTVTMTSTSSVTSSSNVATATTVLSVGQSLNT  LTTSLTSTSSSEDGTQAEYSLYDFLDSCRASLLA  ELDDDEDLPEPDEEDDENEDDQEDQYEEVMILRR  PSLQRRAGSRSDVTHAVTSQLPQVPAGAGSRPIGE  QEEEEYETKGGRRRTWDDDYVLKRQFSALVPAFDPR  PGRTNVQQTDDLEIPPPGTPHSELLEVECTPSRL  ALTLKVTGLGTREVELPLTNFRSTIFYVQKLLQL  SCNGNVKSKDLRIWEPTYTIMYREMKDSDEKENG  KMGCSIEHVEQYLGTDLPKNDLITYLQKNADAA  LRHWKLTGTNKSIRKNRNCSQLIAAYWDLG\EHGK  \SGLNQGAISTLQSSDILNLTKEQPQAKAGNGQNSC  GVEDVLQLLRILYIVASDPYSRISQEDGDEQPQFTF  PPDEFTS/KKITTKILQQIEEPLALASGALPDWCEQ  LTSKCPFLIPFETRQLYFTCTAFGASRAIVWLQNR  EATVERTRTTSSVRDDPGEFVRVGRKHERVKVPRG  ESLMEWAENVMQIHADRKSVLEVEFLGEEGTGLGPT  LEFYALVAAEFQRTDLGAWLCDDNFPDDSRHVDLG  GGLKPPGYVQVRSCLFTAPFPQDSDELERITKLFH  FLGIFLAKCIQDNRLVDLPISKPFKLMCMGDIKSN  MSKLIYESRGDRDLHCTESQSEASTEEGHDSLSVGS  FEEDSKSEFILDPPKPKPPAWFNGLTWEDFELVNP  HRARFLKEIKDLAIKRRQILSNKGLSEDEKNTKLQE  LVLKNPSGSGPPLSIEDLGLNFQFCPSSRIYGFTAV  DLKPSGEDEMITMDNAEYVDFMFCMHTGIQKQM  EAFRDGFNKVFPMEKLSFSHEEVQMILCGNQSPSW  AAEDIINYTEPKLGYTRDSPGFLRFVRVLCGMSSDE  RKAFLQFTTGCSTLPPGGLANLHPRLTVVRKVDATD  ASYPSVNTCVHYLKLPEYSSEEIMRERLLAATMEKG  FHLN</p>
410	302	2179	<p>MSPVFPMILTVMFYIICLRRRARTATRGEMMNTHR  AIESNSQTSPLNAEVVQYAKEVDFSSHYGSENSMS  YTMWNLAGVPNVFPSSGDFQTAVFRYGTWWDQCP  SASLPFKRTPPNFQSQDYVELTFEQQVYPTAVHVLE  TYHPGAVIRILACSANPSPNPPAEVRWEILWSERP  TKVNASQARQFKPCIKQINFPTNLIRLEVNSLLEY  YTELDAVVLHGVDKPVLSLKTSLIDM\NDI\EDDA  YGRKMGCGNGTVLNKKFSS/ALSLGEGPNNGYFDK  LPYELIQLILNHLTLPLDLCLAQTCLLSQHCCDPL  QYIHLNLQPYWAKLDDTSLEFLQSRCTLVQWLNLWS  TGNRGFISVAGFSRFLGFGVSE\LVRLELSCSHFL  NETCLEVISEMCPNLQALNLSCKLPPQAFNHIK</p>

			<p>LCSLKRLVLYRTKVEQTALLSILNFCSELQHLSLGS  CVMIEDYDVIASMIGAKCKLRTLDLWRCKNITENG  IAELASGCPLLEBOLDLWCPTLQSSTGCFTRLAHQL  PNLQKLFILTANRSVCDTDIDEACNCTRLQQLDILG  TRMVSPASLRKLLSECKDLSLLDVSFCSQIDNRAVL  ELNASFPKVFIKKSFTQ</p>
411	1	2975	<p>SLQRLPGLMHNLTFLLDGNFLQSLPAELENMKQLS  YLGLSFNEFTDIEPVLEKLTAVDKLCMSGNCVETLR  LQALRKMPHIKHVDLRLNVIRKLIADVDLQHVTO  LDLRDNKLGDLAMIFNNIEVLHCERNQLVTLDICG  YFLKALYASSNELVQLDVYPVPNYLSYMDVSRNRL  ENVPEWVCESRKLEVLIDIGHNQICELPARLFCNSSL  RKLLAGHNQLARLPERLERTSVEVLVDVQHNQLLELP  PNLLMKADSLRFLNASANKLESPPATLSEETNSIL  QELYLTNNSLTDKCVPLLTGHPHLKILHMAYNRLQS  FPASKMAKLEEEIDLSGNLKAIPPTIMNCRMH  TVIAHSNCIEVFPEVMQLPEIKVDLSCNELSEVTL  PENLPPKLQELDLTGNPRLVLDHKTLELLNNIRCFK  IDQPSTGDASGAPAVWSHGYTEASGVKNKLCVAALS  VNNFCDNREALYGVFDGDRNVEVPYLLQCTMSDILA  EELQKTKNEEYVMNTFIVMQRKLGTAQKLGGA  VLCHIKHDPVDPGGSFTLTSANVGKQTVLCRNGKP  LPLSRSYIMSCEEELKRIKQHKAIITDGVNGVTE  STRILGYTFLHPSVVPVPRHVQSVLLTPQDEFFILGS  KGLWDSLSVEEAVEAVRNVPDALAAAKLCTLAQSY  GCHDSISAVVQLSVTSDSFCCCELSAGGAVPPSP  GIFPPSVNMVIKDRPSDGLGVPSSSSGMASEISSEL  STSEMSSEVGSTASDEPPPGALSSENSPAYPSEQRCM  LHPICLSNSFQRLSSATFSSAFSDNGLSDDEEPI  EGVFTNGSRVEVEVDIHCSRakeKEKQOHLQVPAE  ASDEGIVISANEDEPGLPRKADFSAVGTIGRRRANG  SVAPQERSHNVIEVATDAPLRKPGGYFAAPAQDPD  DQFIIPPELEEEVKEIMKHQEQOQQQPPPPQQLQ  PQLPRHYQLDQLPDYYDTPL</p>
412	86	2034	<p>RMAAILGDTIMVAKGLVKLTQAAVETHLQHLGIGGE  LIMAARALQSTAVEQIGMFLGKVQGDQKHEEYFAEN  FGGPEGEFHFVSVPHAAGASTDFSSASAPDQSAPP  SLGHAHSEGPAPAYVASGPFREAGFPQGASSPLGRANG  RLFANPRDSFSAMGFQRRFFHQDQSPVGGLTAEDIE  KARQAKARPENKQHKQTLSEHARERKVPVTRIGRLA  NFGGLAVGLGFGALAEVAKKSIRSEDPGKKAVALGS  SPFLSEANAERIVRTLCKVRGAALKLGQMLS IQDDA  FINPHLAKIFERVQSAFMPKQMMKTLNNDLGN  WRDKLEYFEERPFAAASIGQVHLARMKGGREVA\MK  IQYPGVAQS INSDVNNLMAVLNMNMLPEGLFPEHL  IDVLRRELALECDYQREAAACARKFRDLLKGHPFFV  PEIVDELCSPHVLTTELVS GFPLDQAEGLSQEIRNE  ICYNILVLCRELFEFHFMTDPNWSNFFYDPQOQHK  VALLDFGATREYDRSFTDLYIQIIRAAADRDRDRETVR  AKSIEMKFLTGYEVKVMEDAHLDAIILGEAFASDE  PFDFTQSTTEKIHNLIPVMLRHLVPPPEETYSLSH  RKMGGSFILCSKLKARFPCKAMFEEAYSNYCKRQAQ  Q</p>
413	2	2913	<p>SQMHCSGLAWHPDIATQLVLCSEDDRLPVIQLWDLR  FASSPLKVLESHSGILSVWSQADAELLLTSAKDS  QILCRNLGSSEVVYKLPTQSSWCFDVQWCFRDPVSF</p>



			<p>SAASFNGWISLYSVMGRSWEVQHMROADKISSFSK  GQPLPPLQVPEQVAQAPLIPPLKKPPKWIRRTGVS  FAFGGKLVTFGLPSTPAHLVPQPCPRLVFISQVTTE  SEFLMRSAEALQEALGSGNLLNYCQNKSSQALLQSEK  MLWQFLKVTLEQDSRMKFLKLLGYSKDELQKKVATW  LKSDVGLGESPOPKGNDLNSDRQQAFCQASKHTTK  EASASSAFFDELVPQNMTPWEIPITKIDGLLSQAL  LLGELGPAVELCLKEERFADAIILAQAGGTDLLKQT  QERYLAKKKTKISSLLACVVQKNWKDVVCTCSLKNW  REALALLLTYSGTEKFPELCDMLGTRMEQEGSRALT  SEARLCYVCSGVERLVECWAKCHQALSPMALQDLM  EKVMVLNRSLEQLRGPHGVSPGPATTYRVTOYANLL  AAQGSLATAMSFLEPRDCAQPPVQQLRDRLEFAQGSA  VLGQQSPFFPFRIVVGVTLHSKETSSYRLGS\QPS  HQVPTPSRPRVFTPOSSPAMPLAPSHSPYQGPRT  QNISDYRAPGPQAIQPLPLSPGVRPASSQPQLLGGQ  RVQVPNPVGFPGTWPLPGSPLEMACPGIMRPGSTSL  PETPRLFLLPLRPLGPGRMVSHTPAPPASFPVPYL  PGDPGAPCSSVLPTTGILTTPHGPQDSWKEAPARG  NLQRNKLPETFMPPAPITAPVMSLTPELQGILPSQP  PVSSVSHAPPGVPGELSLOQLQHLPEKMERKELPP  EHQSLKSSFEALLQRCSLSATDLKTKRKL EEAQRL  EYLYEKLCEGTLSPHVAVAGLHEVARCVDAGSFEQGL  AVHAQVAGCSSFSEVSSFMPIKAVLIIAHKLLV</p>
414	1722	1057	<p>ISLFMG EKRYVKIKIMICHLOLPFFFLNLSISHLH  VPFSFVPQNSRTRDLALANFLLLC THTCRLAPP  /WSTHMTAGAMAGILEHSVMYPVDSVKTRMQSLSPD  PKAQYTSIYGALKKIMRTEGFWRPLRGVNVMMGAG  PAHAMYFACYENMKRTLNDVFHHQGN SHLANGIAGS  MATLLHDAVMNPAEVVKQRLQMYNSQHS AISCI RT  VWRTEGLGAFYRTYNPQLTMNIPFQSIHFITYEFLQ  EQVNP HRTYNPQSHIISGGLAGALAAAATPLDVCK  TLLNTQENVALSLANISGRLSGMANAFRTVYQLNGL  AGYFKGIQARVIYQMPSTAISWSVYEFFKYFLTKRQ  LENRAPY</p>
415	54	2891	<p>SKKMVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQ  STEASPKRSDGTPFPWNKIRLPEYVIPVHYDLLIHA  NLTTLTFWGTTKVEITASQPTSTIILHSHLQISRA  TLRKGAGERLSEEPLOVLEHPPQE QIALLAPEP\LF  VGLPYTVVIHYAG\NLSETFHGFYKSTYRTKEGELR  ILASTQFEPTAARMAFP CFDEPAFKASFSIKIREP  RHLAISNMPLVKSVTVAEGLIEDHF\DVVPKMSTYL  VAFIISDFESVSKITKSGVKVSVYAVDPKINQADYA  LDAAVTLLEFYEDYFSIPYPLPKQDLAAIPDFQSGA  MENWGLTTYRESALLFDAEKSSASSKLGITVTV AHE  LAHQWFGNLVTMEWWDNLWLN EGF AKFMEFVS SVT  HPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENP  AQIREMFDDVSYDKGACILNMLREYLSADAFKSGIV  QYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDGFC  SRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLIT  ITVRGRNVHMKQEHYMKSGD GAPDTGYLWHVPLTFI  TSKSDMVHRFLLKTKTDVLLP EEWIKFNVGMNG  YYIVHYEDDGWDSL TGLLKGTH TAVSSNDRASLINN  AFQLV SIGKLSIEKALDLSLYLKHETEIMPVFQGLN  ELIPMYKLM EK RDMNEVETQFKAFLIRLLRDLIDKQ  TWTDEGSVSEQMLRSELLLLACVHNYQPCVQRAEGY  FRKWESNGNLSLPVDVTLAVFAVGAQSTEGWDFLY</p>

			SKYQFSLSTEKSQIEFALCRTQNKELQWLLDESF KGDKIKTQEFQILTLIGRNPVGYPLAQFLRKWN KLVQKFELGSSSIAHVMGTNQNQFSTRLEEVKGF FSSSLKENGSQLRCVQQTIEETIEENIGWMDKNFDKIR VWLQSEKLERM
416	1079	1061	FFVFLVETGFHRVSQDGLDLLTS*STCLGLPKCDY RCEPPRANSTNS*ELAQ
417	353	3	DEKPLPRALQCPPLHSAPSTPLKFCP*ATGRRPFAP SPTHPSLRPPPSLPTCFLPPVPVFHEAAVSPCPCLA TLRWAPPPRLSLAGVRQSPAEGGRVLGDPPELPPRI PPQGLYSR
418	236	1126	CLASRLPCALTMPAATVDHSQRICEVWACNLDEEMK KIRQVIRKYNVAMDTEFFGVVARPIGEFRSNADYQ YQLLRNCVDDLKIIQLGLTFMNEQGEYPPGTSTWQF NFKFNLTEDMYAQDSIELLTSGIQFKHEEGEGET QYFAELMTSGVVLCEGVKWSFHSGYDFGYLIKIL TNSNLPEBELDFFEILRLFFPVIYDVKYLKMSCKNL KGGQLQVAEQLELERIGPQHAGSDSLTGMMAFFKM REMFEDHIDDAKYCGHLYGLSGSSSVQNGTGNAY EEEEANKOS
419	201	636	RRLRERDRVSGEGGRPRAGISEALRCIMKFPQYKEDH PFYRKKEGEEKIRKKYPDRVPVIVEKAPKARVPDL KRKYLVPSDLTVGQFYFLIRKRIHLRPEDALFFVFN NTIPTSATMGQLYEDNHEEDYFLYVAYSDESVMYK
420	1	1638	FRPTVPSPVSMVWIPCAVASFFGDASAAWGGELS GSYTATARMDRMTEDALRLNLKRSLLDPADERDDVL AKRLKMEGHEAMERLKMALALKRKDLANLEVPHELP TKQDGSQVKGYYEKLNGNLRPHGDNRTAGRPGKENI NDEPVDMSARRSEPERGRLTPSPDIIVLSDNEASSP RSSSRMEERLKAANLEMFKGKGIERQQLIKQLRDE LRLEEARLVLLKLRQSQLQKENVVQKTPVVQNAAS IVQPSPAHVGQQLSKLPSRPGAQGVPEQNLRTLQG HSVIRSATNTTLPHMLMSQRVIAPNPAQLQGQGGPP KPGLVRTTTPNMNPAINYQPQSSSVPCQRTTSSAI YMNLAHQPGTVNRVSSPLSPSAMTDAANSQAAA KLALRKQLEKTLLEIPPPKPPAPLLHFLPSAANSEF IYMGLEEVVQSVIDSQKSCASLLRVEPFVCAQCR TDFTPHWKQEKNGKILCEQCMTSNQKALKAEHTNR LKNAFVKALQQEQVRILTAHWPPVPVCFQRVAPSS LQEWFM
421	47	454	RCRSYEDCCGRCCVRALSIQRLWYFWFLMMGVLF CCGAGFFIRRRMYPPPLIEEPAFNVSYTRQPPNPGP GAQQPGPPYYTDPGGPGMNPVGNMAMAFQVPPNSP QGSVACPPPPAYCNTPPPPYEQVVKAK
422	81	621	ITMGNIFEKLFKSLGKKMRILILSLDTAGKTTIL YKLLGETVPAVPTVGFCVETVEYKNNTFAVWDVGS HFKIRPLWQHFFQNTKGARSPGSTHQGSLASGVLPI KCSHVEFGMWKGRSHPFPLPHSSRCAGSGGQLDSIL PHQSPAAGPWGCKDLSSGFPSFLTSSILWKS AVVK
423	2	4030	RHPGCGAGRPGAPPPRHGSRGGRGDRARAGGGGFSR GSGGGGGRGLRADGRAPGLRGLGAAPHCAGLGPGA MSGGGGGGGSAPSRFADYFVICGLDTETGLEPDELS ALCQYIQASKARDGASPFISSTEGENFEQTPLRRT FKSKVLARYPENVEWNPFDQDAVGMLCMPKGLAFKT QADPREPQFHAFIITREDGSRFTGFALTFYEEVTSK QICSAMQTLYHMNAEYDVLHAPPADDRDQSSMEDG

			EDTPVTKLQRFNSYDISRDTLYVSKCICLITPMSEFM KACRSVLEQLHQAVTSPQPPPLPLESYTYNVLYEVP LPPPGRSCLKFSGVYGPIICQRPSTNELPLFDFPVKE VFELGVENVFQLFTCALLEFQILLYSQHYQRLMTV AETITALMFPFQWQHVVVPILPASLLHFLDAPVPYL MGLHSNGLDDRSKLELPQEANLCFVDIDNHFIELPE DLPQFPNKLEFVQEVSEILMAFGIPPEGNLHCSESA SKLKRRLASELVSDKRNGNIAGSPLHSYELLKENET IARLQALVKRTGVSLEKLEVREDPSSNKDLKVQCDE EELRIYQLNIQIREVFANRFTQMFADEYEVFVIQPSQ DKESWFTNREQMNFQDKASFLSDQPEPYLPFLSRFL ETQMFASFIDNKIMCHDDDDKDPVLRVFSRVDKIR LLNVRTPTLRTSMYQKCTTVDEAEKAIELRLAKIDH TAIHPhLLDMKIGQGYEPGFPPKQSDVLSTGPPAS NKWTKRNAPAQWRRKDRQKQTEHLRLDNDQREKYI QEARTMGSTIRQPKLSNLSPSVIAQTNWKFVEGLLK ECRNKTKRMLVEKMGREAVELGHGEVNITGVEENTL IASLCDLLERIWSHGLQVKQKGSALWSHLLHYQDNR QRKLTSGSLSTSGILLDSERRKSDASSLMPELRISL IQDMRHIQNIKEIKTDVGKARAWVRLSMEKKLSRH LKQLSDHELTKKLYKRYAFLRCDDEKEQFLYHLLS FNAVDYFCFTNVFTTILIPYHILIVPSKKLGGSMT ANPWICISGELGETQIMQIPRNVLEMTFECQNLGKL TTVQIGHDNISGLYAKWLVEYVMVRNEITGHTYKFC GRWLKGMDGSLERILVGEELTSQPEVDERPCRT PLQQSPSVIRRLVTISPNNKPKLNTGQIQESIGEAV NGIVKHFHKPEKERGSLTLLCGECGLVSALEQAFQ HGFKSPRLFKNVFIWDFLEKAQTYETLEKNEVVPE ENWHTRARNFCRFVTAINNTPRNIGKDGKFMVLVCL GARDHLLHHWIALADCPITAHMYEDVALIKDHTLV NSLIRVLQTLQ
424	2	1671	LADGDMPLPILLPLPWWGGSLOQKPVYELQVQKSVTV QEGCLVLVPCSFSPWRSWYSSPPLYVYVFRDGEIP YYAEVVATNNPDRRVKQPETQGRFRLLDVQKKNCSL SIGDARMEDTGSYFFRVERGRDVKYSYQKNLNEV TALIEKPDIFLEPLESGRPTRLSCSLPGSCEAGPP LTFWSWTGNALSPDPETTRSELTLTPRPEDHGTNL TCQMKRQGAQVTTERTVQLNVSYAQTTITIFRNGIA LEILQNTSYLPVLEGAALRLCDAPSNPPAHLWFQ GSPALNATPISNTGILELRRVRSAAEGGFTCRAQHP LGSLLQIFLNLVSVSLPQLLGPSCSWEAEGHCRCSF RARPAPSLCWRLEEKPLEGNSSQGSFKVNSSSAGPW ANSSILHGGSLSDLVKVSCKAWNIYGSQGSVLLQ GRSNLGTGVVPAALGGAGVMALLCICLCIFFLIVK ARRKQAAGRPEKMDDEDPIMGTITSGSRKKPWPDPSP GDQASPPGDAPPLEEQKELHYASLSFSEMKSREPKD QEAPSTTEYSEIKTSK
425	3	342	HAGCQFKALLWKNWLCRLRNVLFLAEFFWPCILFV ILTVLRFQEPFRYRDICYLQPRDLPCSGVIFPVQSL LCNTGSRCRN\SAMKGQWSIIFGKRNTKIFFRNLRK LIHRTG
426	3	313	QYDPEDKTQSEQWLPTGRSGPVKAKEVQSRKVMAG VFWDAQGNMPADFLGQRTITSAYYEMTWRLAK\V LAEKHPGKLLQRVLLNHDNVLAHYSHQTRAF
427	1	413	RQSSRDHTIPSLRVY*HSES*GYSVYLLKNFYSMKL ALETTLCALFLRLQQLLHQRTHPVFITHIRAHSSLP

			GPLAYGNDQAALQVVTSLLDQATQLHQFFYN*/QK LILNNFNLYR/ELAKQII*RCPCQLTGTAPL
428	774	3148	NINRKLFPFPPLDSGYTLFAICEISPWLDRGISEPEC SSEQHPEVSITLLPVEPMTSDQDAKVVAEPQTQRVQ EGKDSAHLMNGPISQTTSTSSIPPLSQVPATKVSE LNPNAEVWVWAPVLHLEASSAADGVSAWEEVAGHHA DRGPQGS DANGDGDQGHENAALPDPQESDPADMNAL ALGPSEYDSL PENSETGGNESQPDSDQEDPREVLKKT LEFCLSRNLASDMYLISQMDSDQYVPITTVANLDH IKKLSTDVDLIVEVLRSLPLVQVDEKGEKVRPNQNR CIVILREISESTPVEEVEALFKGDNLPKFINCEPAY NDNWFITFETEADAQQAYKYLREEVKTFFQKPIKAR IKAKAIAINTFLPKNGFRPLDVSLYAQQRYATSFYF PPMYSPOQQFPLYSLITPQTWSATHSYLDPPLVTPF PNTGFINGFTSPAFAKPAASPLTSLRQYPPRSRNPSK SHLRHAIPSAERGPGLLESPIFNFTADRLINGVRS PQTRQAGQTRTRVQNPSAYAKREAGPGRVEPGSLES SPGLGRGRKNSFGYRKKREEKFTSSQTQSPTPPKPP SPSFELGLSSFPPLPGAAGNLKTEDLFENRLSSLI I GPSKERTLSADASVNTLPVVVSREPSVPASCAVSAT YERSPPAHL PDDPKVAEKQRETHSVDRLP SALTAT ACKSVQVNGAATELRKPSYAEICQRTSKEPPSSPLQ PQKEQKPNTVCGGKEEKLAEPAERYREPPALKSTP GAPRDQRRPAGGRPSPSAMGKRLSREQSTPPKSPQ
429	3112	2204	SAIVPGPGLERVHWGRPCAPAPRKMPDQALQQMLDR SCWVCFATDEDDRTAEWVRPCRCRGSTKWVHQACLO RWVDEKQRGNSTARVACPQCNAEYLIVF PKLGPVVY VLDLADRLISKACPF AAAGIMVGSIIYTAITYGAVT VMQVVGHKEGLDVMERADPLFLLIGLPTIPVMLILG KMIRWEDYVLR LWRKYSNKLQILNSIFPGIGCPVPR IPAEANPLADHVSATRILCGALVFPTIATIVGKLMF SSVNSNLQRTILGGIAFVAIKGAFKVYFKQQQYLRQ AHRKILNYPEQEEA
430	3	332	KISACFTKGAA*NTGTIQK/TSAILQPHAEVSLKKG C*RKSSA*A*LQAMYL VVCSTWRERWPEVQIYTDL* VVTNSLIVC*G\**KKND*KSVDEKI*GTGM*TDLS NWA
431	2	529	AWRAGRRRRVQGNSGLQSPCWGFRERLDPGFWDAS GEGSTGFAFIRPKMPFFGNTFS PKKTPPRKSASLSN LHSLDRSTREVELGLEYGSP TMNLAGQSLKFENGQW IAETGVSGGVDRREVQRLRRRNQOLEEENNLRLKV DILLDMLSESTAESHMEKELDELRI SRKRK
432	7	652	GRGREVQPPSPAFFGAQPRRGRGRGESADGAMREY KVVVLGSGGVGKSALT VQFVTGSFIEKYDPTIEDFY RKEIEVDSSPSVLEILD TAGTEQFASMRDLYIKNGQ GFILVYSLVNQQSFQDIKPMRDQIIIRVKRYERVPMI LVGNKVDLEGEREVSYGEGKALAEWSCP FMETSAK NKASVDELFAEIVRQMNYYAQPNGDEGCCSACVIL
433	3	974	TIRSTDPVMSQCACLEEVHLEPNIKPGEGLGMYIKS TYDGLHVITGTTENS PADRSQKI HAGDEVIQVNQQT VVGWQLKNLVKKLRENPTGVVLLLKKRPTGSFNFT APLKNLRW\K PPLVQTSPPPATTQSPESTMDTSLKK EKSAILDLIYIPPPAVPYSPRDENG SFVYGGSSKCK QPLPGPKGSESPNSFLDQESRRRRFTIADSDQLPGY SVETNILPTKMREKTPSYGKPRPLSMPADGNWMGIV DPFARPRGHGRKGEDALCRYFSNERIPPIIESSSP

			PYRFSRPTTERHLVRGADYIRGSRCYINSDLHSSAT
434	3	1062	PTIRHEGWKGCTCTFKDRSKLREHLRSHTQEKVVAC PTCGGMFANNTKFLDHIRRQTSLDQQHFQCSHCSKR FATERLLRDHMRNHVNHKPLCDMTCPLPSSLRNH MRFRHSEDRPFKDCDDYCKNLIDLQKHLDTHEE PAYRCDFENCTFSARSLCSIKSHYRKVHEGDSEPRY KCHVCDKCFTRGNNLTVHLRKKHQFKWPSGHPFRFY KEHEDGYMRLQLVRYESVELTQQLLRQPQEGSGLGT SLNESSLQGIILETVPGEPGRKEEEEEEGKGSEGTAL SASQDNPSVHVVNQTNAGQQQEIIVYVYLSEAPGE PPPVPPEPPSGGIMEKLQGI AEPEIQMV
435	2435	925	RVWTLWGLLFFGNLLPFPGWCCQEGPSEGCNLFW RQVLAWPGSSTMFLLLPFDLSLIVNLLGISLTVLFTL LLVFIIVPAIFGVSGIRKLYMKSLKIFAWATLRM ERGAKEKNHQLYKPYTINGIIAKDPTSLEEEIKEIRR SGSSKALDNTPEFELSDIFYFCRKGMEITIMDDEVTK RFSAEELSWNLLSRTNYNFYISLRLTVLWGLGLV IRYCFLLPLRIALFTGISLLVVGTTVVGYLPNGRF KEFMSKHVHLMCYRICVRLTAIITYHDRENRPNG GICVANHTSPIDVIIASDGYAMVGQVHGGLMGVI QRAMVKACPHVWFERSEVKDRHLVAKRLTEHVQDKS KLPIILIFPEGTCINNTSVMFCKGSFEIGATVYPVA IKYDPQFGDAFWNSSKYGMVTYLLRMMTSAIVCSV WYLPMTREADEDAVQFANRVKSAIARQGGVLVDLLW DGLKREKVKDTFKEEQQLYSKMIIVGNHKDRSRS
436	11	1835	EVREGGGKEEEAGSGRCVCGGLAPKGRPRRRADPVA SAIMDPVEAVLQEKALKFMNSSEREDCNNGEPPrKI IPEKNSLRQTYNSCARLCLNQETVCLASTAMKTENC VAKTKLANGTSSMIVPKQRKLSASYEKEKELCVKYF EQWSESDQVEFVEHLISQMCHYQHGHINSYLPMLQ RDFITALPARGLDHIAENILSYLDAKSLCAELVCK EWYRVTSBGMLWKKLIERMVRTDSLWRGLAERRGWG QYLFKNKPPDGNAPPNSFYRALYPKIIQDIETIESN WRCGRHSLQRIHCRSETSKGVYCLQYDDQKIVSGLR DNTIKIWDKNTLECKRILTGHTGSVLCLOQYDERVII TGSSDSTVRVWDVNTGEMLNTLIHCEAVLHLRFNN GMMVTCCKDRSIAVWDMASPTDITLRRVLVGHRAAV NVVD FDDKYIVSASGDRTIKVWNTSTCEFVRTLNGH KRGIACLQYRDLVVSGSSDNTIRLWDIECGACLRV LEGHEELVRCIRFDNKRIVSGAYDGKIKVWDLVAAL DPRAPAGTLCRLTLVEHSGRVFRLQFDEFQIVSSSH DDTILIWDFLNDPAAQSEPPRSPSRITYTISR
437	1425	817	TISSGQPSVISWRFPFGHSGWHEYVLSCWDSWLLNF SSFFQAGKGDVLGWRLGAGHHISLRGKSRLKSDFS VSTICAIDFFLMGLAVTFLSETFLSSAQKRGRGGES DLEPIDSWLITQGMIPVAQPSVMDDIEVWLRTDLKG DDLEEGVTSEEDKFLEERAKAAEMVDPDLPSPMEA PAPASNPSGRKKPERSEDALFAL
438	227	1519	VTLIKMNAMLETPELPAVFDGVKLA AVAVLYVIVR CLNLKSPTAPPDLYFQDSGLSRFLKSCPLLTKEYI PPLIWGKSGHIQTALYGMGRVRSPPHYGHRKFITM SDGATSTFDLFEPLAEHCVGDDITMVICPGIANHSE KQYIRTFVDYAQKNGYRCVILNHLGALPNIELTSPR MFTYGTWFEFGAMVNYIKKTYPLTQLVVVGFSLGGN IVCKYLGETQANQEKVLCCVSVCQGYALRAQETFM QWDQCRRFYNFLMADNMKKIILSHRQALFGDHVKKP

			QSLEDTDLRLYTATSLMQIDDNVMRKFHGYNSLKE YBEEESCMRYLHRIYVPLMLVNAADDPLVHESILTI PKSLSEKRENVFVLPPLHGGHLGFFEGSVLFPEPLT WMDKLVEYANAICQWERNKLQCSDETEQVEADLE
439	76	764	KTVDQMQRLLLLPFLLLGTVSALHLENDAPHLESLET QADLGQDLDSSEKERDIALTEEVIAEGEEVKASA CQDNFEDEEAMESDPAALDKDFQCPREEDIVEVQGS PRCKTCRYLLVTRPKTFAEQNVCSRCYGGNLVSIH DFNFNYRIQCCTSTVNQAQVWIGGNLRGWFLWKRFC WTDGSHWNFAYWSPGQPGNGQGSCVALCTKGGYWRR AQCDKQLPFVCSF
440	136	225	KLTEKIKEERIHCNSIYKASITLLTKVDS
441	580	806	FPEEPQSPAHPGAKHRGTSPAQVGLSGRGHPTSAWS GHWQPRWRFLAQSLRGNG*RGGR*LPGS*WGCNS RESRGHQGPPKAVPGAG*EKSWGSPGGHGEDGIYE ATRFPGIPG*RAHVRPG/PR/REAPPGPVPPHP PGTKSAASHQSSMTSLESGISERLPQKPLHRGGGP HLEETWMASPETDSGFVGSETSRVSLTQTPEHRLS HISTAGTLAQFPAASVPRDGASYPKARGSLIPRAT EPSTPRSQAQRYLSSPSGPLRQAPNFSLETLAAE MAVPGSEFEGHKRISEQPLPNKTISPPAPAPA
442	164	489	VDNSNLSLNMASQKRTNRCERKQLTGQNTATKHEPA P/WNYKNTYGSSTIRTTKAPGESTNAAPHYHKLCR VSHIWGNRRGQHIWNAMDKPRP*\KNAFMIMVSPVD AA
443	736	17	*RAMNFSICFLEIGSI*TRYCKTVLCKLRAVL*SF RVLNITKAYLVLFSSLYKNLICSSVRSVPLKKFLKS LSSILRDRFFK*T*NPRGERERVLLGDFE*DRFRKC LSLILPGGECSSDLLRTSPSLTALPPNSIHCCSDPC ITSINLEPIKLL*HLRPPEASTHEANFTMASPLFRP S*CFKKITPSTHKPEKTRTSSSFTR*GKPRRNK*G FSAFNGLVFLGLKLPVPLV*NP
444	1350	1499	GGSSPGNTAGCPSGNGGNAAPYGAEGVRPPPGPAP LPPGPTKPLPPAPP
445	1	339	VKMGH*SLDPEIPTKSKSRGSLLDHFKNARETAQ AIKGMHT*EVTKCLKDVPL*KQCMFRLGRGGAGRC T*AKQWGWTOGW*PEKSAEFLHTIKNVESHTCEG VDVGS
446	2	131	AAAQQRSHPAMSPGTPGPTMGRSQGSPMDPMVMKRP QLYGMGSNPHSQPQQSSPYPGGSYGPPGPQRYPIGI QGRTPGAMAGMQYPQQMPQYGOQGVSGYCQQGQQ PYYSQQPQPHLPPQAQYLPQSQQRYQPQDMSQE GYGTRSQPSSGPRKT*PGDEPRHPRTDHGQIPGQPN GSNGDEETSUVWHGQ
447	1	562	LLKSSEKKLQETPTEANHVQRLRQMLACPPHGLLDR VITNVTIIVLLWAVVWSITGSECLPGGNLFGIILF YCAIIGGKLLGLIKLPTLPLPSLLGMLLAGFLIRN IPVINDNVQIKHKWSSSLRSIALSIILVRAGLGLDS KALKKLKGVCVRLSMGPCIVEACTSALLAHYLLGLP WQWGFIL
448	384	232	FRLLICEISLLYFSADIYTFVCVYVCLSMF*SYCKLA F*K*ILVLD*SVLV*
449	43	762	SSILQIYDLCDALSPTFYFLLPSSKIRDVTFLENE EGKNIIVIMSSAGYIYTQLMEEASSAQGPYVTNV LEINHEDLKDSNSQVAGGGVSVYSHVLQMLFFSYC QGSFAATISRTTLEVLQFPINIKSSNGGSKTSPA

			LCQWSEVMNHPGLVCCVQQTGVPPLVVMVKPDTFLI QEIKTLPAKAKIQDMVAIRHTACNEQQRTTMILLCE DGSLRIYMANVENTSYWLQPSLQP
450	57	558	TRAGVEGAGTWGARRVAIAGGTSGAAATDNAVATS VSMMDLVLEEDVTVPGTSLGCSGLVPSVPDDLGIN PNAGLGNGLLPNVSEETVSPTRARNMKDFENQITEL KKENFNLKLRIYFLEERMQQEFHGPTTEHYKTNIEL KVEVESILKRELQEREQLLIKAS
451	36	635	TNELIHRPQPDSSQQRFPVPTPAKRSARAPSLPAGH LASLPATMPNVLLPPKESNLFKRILKCYEQKQYKNG LKFCMKILSNPKFAEHGETLAMKGLTLNCLGKKEEA YEFVRKGLRNDVKSHVCWHVYGLLQRSCLKYDEAIK CYRNALKLDKDNLQILRDLSLLQIQMRDLEGYRETR YQLLQLRPTQRASWIGYAI
452	43	1743	DLFIIDQIKFIMDSL NKEPFRKNYNLITFDSLEPMQ LLQVLSVDLAEIDPKQLVDIREEMPEQTAKRMLSL GILKYKPSGNATDMSTFRQGLVIGSKPVIYPVLHWL LQRTNELKKRAYLARFLIKLEVPSEFLQDETVDATN KQYEELMEAFKTLHKEYEQLKISGFSTAEIRKDISA MEEKDQLIKRVEHLKKRVETAQNHQWMLKIARQLR VEKEREYLAQQQEQKNQLFHAVQRLQRVQNQLKS MRQAAADAKPESLMKRLEEEIKFNLYMGTEKFPKEL ENKKKELHFLQKVVSEPAMGHSDDLLELESKINEINT EINQLIEKKMRNEPIEGKLSLYRQQASIISRKKEA KAEELQEAKEKLASLEREASVKRNQTRFDGTEVLK GDEFKRYVNKLRSKSTVFKKKHQIIAELKAEFGLLQ RTEELLKQRHENIQQLQTMEEKKGISGYSYTQEEL ERVSALKSEVDEMKGRTLDDMSEMVKKLYSLVSEKK SALASVIKELRQLRQKYQELTQECDEKKSQYDSCAA GLESNRSKLEQEVRLREECLQESRY

#### 4.5 EXAMPLE 5

##### Novel Nucleic Acids

Using PHRAP (Univ. of Washington) or CAP4 (Paracel), a full length gene cDNA  
sequence and its corresponding protein sequence were generated from the assemblage. Any  
frame shifts and incorrect stop codons were corrected by hand editing. During editing, the  
sequence was checked using FASTY and/or BLAST against Genbank. Other computer  
programs which may have been used in the editing process were phredPhrap and Consed  
(University of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq, Inc.). The full-length  
nucleotide sequences, including splice variants resulting from these procedures are shown in  
the Sequence Listing as SEQ ID NOS: 453 – 455. The amino acids are SEQ ID NO:478 –  
480 respectively.

The nearest neighbor results for SEQ ID NO: 453-455 were obtained by a  
FASTA version 3 search against Genpept release 117, using FASTXY algorithm.

FASTXY is an improved version of FASTA alignment which allows in-codon frame shifts. The nearest neighbor result showed the closest homologue for SEQ ID NO: 453-455 from Genpept. The nearest neighbor results for SEQ ID NO: 453 -455 are shown in Table 7 below.

#### 5           4.6 EXAMPLE 6

##### Novel Nucleic Acids

Using PHRAP (Univ. of Washington) or CAP4 (Paracel), a full length gene cDNA sequence and its corresponding protein sequence were generated from the assemblage. Any frame shifts and incorrect stop codons were corrected by hand editing. During editing, the sequence was checked using FASTY and/or BLAST against Genbank (i.e., dbEST version 10   117, gb pri 117, UniGene version 117, Genpept release 117). Other computer programs which may have been used in the editing process were phredPhrap and Consed (University of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq, Inc.). The full-length nucleotide sequences including splice variants resulting from these procedures are shown in the Sequence Listing as SEQ ID NOS: 456-471. The amino acids are SEQ ID NO: 481-496 15   respectively.

The nearest neighbor results for SEQ ID NO: 456 – 471 were obtained by a BLASTP version 2.0al 19MP-WashU search against Genpept release 118, using BLAST algorithm. The nearest neighbor result showed the closest homologue for SEQ ID NO: 20   456-471 from Genpept. The nearest neighbor results for SEQ ID NO: 456-471 are shown in Table 7 below.

#### 4.7 EXAMPLE 7

##### Novel Nucleic Acids

25       Using PHRAP (Univ. of Washington) or CAP4 (Paracel), a full length gene cDNA sequence and its corresponding protein sequence were generated from the assemblage. Any frame shifts and incorrect stop codons were corrected by hand editing. During editing, the sequence was checked using FASTY and/or BLAST against Genbank (i.e., dbEST version 117, gb pri 117, UniGene version 117, Genpept release 117). Other computer programs 30   which may have been used in the editing process were phredPhrap and Consed (University



of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq, Inc.). The full-length nucleotide sequences, including splice variants resulting from these procedures are shown in the Sequence Listing as SEQ ID NOS: 472-474. The amino acids are SEQ ID NO: 497-499 respectively.

5       The nearest neighbor results for SEQ ID NO: 472 – 474 were obtained by a BLASTP version 2.0a1 19MP-WashU search against Genpept release 118, using BLAST algorithm. The nearest neighbor result showed the closest homologue for SEQ ID NO: 472 – 474 from Genpept. The nearest neighbor results for SEQ ID NO: 472-474 are shown in Table 7 below.

10

#### 4.8 EXAMPLE 8

##### Novel Nucleic Acids

Using PHRAP (Univ. of Washington) or CAP4 (Paracel), a full length gene cDNA sequence and its corresponding protein sequence were generated from the assemblage. Any  
15   frame shifts and incorrect stop codons were corrected by hand editing. During editing, the sequence was checked using FASTY and/or BLAST against Genbank (i.e., dbEST version 118, gb pri 118, UniGene version 118, Genpept release 118). Other computer programs which may have been used in the editing process were phredPhrap and Consed (University of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq, Inc.). The full-length nucleotide  
20   sequences, including splice variants resulting from these procedures are shown in the Sequence Listing as SEQ ID NOS: 475 and 476. The amino acids are SEQ ID NO: 500 and 501 respectively.

The homology for SEQ ID NO: 475 and 476 were obtained by a BLASTP version 2.0a1 19MP-WashU search against Genpept release 118, using BLAST algorithm. The  
25   results showed homologues for SEQ ID NO: 475 and 476 from Genpept. The homologues with identifiable functions for SEQ ID NO: 475 and 476 are shown in Table 7 below.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), all the  
30   sequences were examined to determine whether they had identifiable signature regions. Table 8 shows the signature region found in the indicated polypeptide sequences, the

description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

#### 4.9 EXAMPLE 9

##### 5 Novel Nucleic Acids

Using PHRAP (Univ. of Washington) or CAP4 (Paracel), a full length gene cDNA sequence and its corresponding protein sequence were generated from the assemblage. Any frame shifts and incorrect stop codons were corrected by hand editing. During editing, the sequence was checked using FASTY and/or BLAST against Genbank (i.e., dbEST version 10 119, gb pri 119, UniGene version 119, Genpept release 119). Other computer programs which may have been used in the editing process were phredPhrap and Consed (University of Washington) and ed-ready, ed-ext and gc-zip-2 (Hyseq, Inc.). The full-length nucleotide sequence, including splice variants resulting from these procedures is shown in the Sequence Listing as SEQ ID NO: 477. The amino acid is SEQ ID NO: 502.

15 The homology for SEQ ID NO: 502 were obtained by a BLASTP version 2.0a1 19MP-WashU search against Genpept release 119, using BLAST algorithm. The results showed homologues for SEQ ID NO: 502 from Genpept. The translated amino acid sequences for which the nucleic acid sequence encodes are shown in the Sequence Listing. The homologues with identifiable functions for SEQ ID NO: 502 are shown in Table 7 20 below.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), all the sequences were examined to determine whether they had identifiable signature regions. Table 8 shows the signature region found in the indicated polypeptide sequences, the 25 description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

TABLE 7 (BLAST)

SEQ ID NO:	SEQ ID NO.	ACCESSION NUMBER	DESCRIPTION	SMITH-WATERMAN SCORE	% IDENTITY
453	784CIP2_180	X55681	Lycopersicon esculentum extensin (Class I)	173	34.524
454	784CIP2_213	D86971	Homo sapiens no similarities to reported gene products	4510	100.000
455	784CIP2_267	Z82244	Homo sapiens bK286B10.1	288	61.176
456	784CIP2B_77	AL163206	Homo sapiens protein with homology to KIAA0790	1944	100
457	784CIP2B_23 1	M28515	Mus musculus zinc finger protein mfg3	225	28
458	784CIP2B_27 1	AC002464	Homo sapiens organic cation transporter; 50% similarity to JC4884 (PID:g2143892)	1542	99
459	784CIP2B_30 7	AJ011863	Homo sapiens homeobox protein LSX	3841	99
460	784CIP2B_33 3	AB032957	Homo sapiens KIAA1131 protein	8443	100
461	784CIP2B_34 1	AL022395	Homo sapiens dJ273N12.1 (PUTATIVE protein based on EST matches)	3287	100
462	784CIP2B_34 2	AL022395	Homo sapiens dJ273N12.1 (PUTATIVE protein based on EST matches)	2403	83
463	784CIP2B_34	AB023624	Rattus norvegicus	4792	92

SEQ ID NO:	SEQ ID NO.	ACCESSION NUMBER	DESCRIPTION	SMITH-WATERMAN SCORE	% IDENTITY
	8		SCOP		
464	784CIP2B_400	AL080141	Homo sapiens hypothetical protein	4793	99
465	784CIP2B_481	AF106037	Homo sapiens adipocyte-derived leucine aminopeptidase	4905	99
466	784CIP2B_597	AB041648	Mus musculus unnamed protein product	625	100
467	784CIP2B_598	AB032976	Homo sapiens KIAA1150 protein	1929	100
468	784CIP2B_694	U88573	Homo sapiens NBR2	566	92
469	784CIP2B_742	AK000452	Homo sapiens unnamed protein product	1473	100
470	784CIP2B_918	Z48745	Mus musculus ABC8	1101	69
471	784CIP2B_1093	AK001122	Homo sapiens unnamed protein product	227	43
472	784CIP2C_37	AB018339	Homo sapiens KIAA0796 protein	5532	99
473	784CIP2C_38	AB018339	Homo sapiens KIAA0796 protein	5497	98
474	784CIP2C_131	AF041206	Homo sapiens midline 1 cerebellar isoform 1	212	42
475	784CIP2D_88	U23084	Saccharomyces cerevisiae Yn10453p	102	23
476	784CIP2D_91	AF106682	Homo sapiens spindlin	933	75

SEQ ID NO:	SEQ ID NO.	ACCESSION NUMBER	DESCRIPTION	SMITH-WATERMAN SCORE	% IDENTITY
477	784CIP2E_3	AF043222	Dreissena polymorpha foot protein 1 precursor	121	37

TABLE 8 (eMatrix)

SEQ ID NO.	SEQ ID NO:	ACCESSION NUMBER	DESCRIPTION	RESULTS*
475	784CIP2D_88	PR00785	NUCLEAR TRANSLOCATOR SIGNATURE	PR00785H 15.80 8.244e-08 85-102
476	784CIP2D_91	PR00539	MUSCARINIC M2 RECEPTOR SIGNATURE	PR00539E 9.66 4.490e-08 207-227
477	784CIP2E_3	PR00519	5-HYDROXYTRYPTAMINE 5B RECEPTOR SIGNATURE	PR00519A 8.06 8.403e-06 36-53

5

\*results include in order: accession number subtype; raw score; p-value; position of signature in amino acid sequence.

Table 5 provides a correlation between the amino acid sequences set forth in the sequence listing, and the nucleotide sequence encoding the amino acid sequence.

10

TABLE 5

SEQ ID NO: OF NUCLEIC ACIDS	SEQ ID NO: OF POLY-PEPTIDE	SEQ ID NO: OF CONTIG NUCLEIC ACIDS	SEQ ID NO: OF CONTIG POLY-PEPTIDE	SEQ ID NO: OF CONTIG IN U.S.S.N. 09/488,725	SEQ ID NO: OF FULL-LENGTH NUCLEIC ACIDS	SEQ ID NO: OF FULL-LENGTH POLY-PEPTIDE	DOCKET NO FULL-LENGTH SEQUENCE_ SEQ ID NO: IN APPLICATION
1	114	227	340	10005			
2	115	228	341	10030			
3	116	229	342	10045	471	496	784CIP2B_109 3
4	117	230	343	10066			
5	118	231	344	10133	475	500	784CIP2D_88
6	119	232	345	10159	476	501	784CIP2D_91
7	120	233	346	10272			

SEQ ID NO: OF NUCLEIC ACIDS	SEQ ID NO: OF POLY- PEPTIDE	SEQ ID NO: OF CONTIG NUCLEIC ACIDS	SEQ ID NO: OF CONTIG POLY- PEPTIDE	SEQ ID NO: OF CONTIG IN U.S.S.N. 09/488,725	SEQ ID NO: OF FULL- LENGTH NUCLEIC ACIDS	SEQ ID NO: OF FULL- LENGTH POLY- PEPTIDE	DOCKET NO FULL-LENGTH SEQUENCE_ SEQ ID NO: IN APPLICA- TION
8	121	234	347	1163			
9	122	235	348	1258			
10	123	236	349	1281			
11	124	237	350	1450			
12	125	238	351	1608			
13	126	239	352	1619			
14	127	240	353	1621			
15	128	241	354	1626			
16	129	242	355	1628			
17	130	243	356	1757			
18	131	244	357	1806			
19	132	245	358	1889			
20	133	246	359	1921			
21	134	247	360	1928			
22	135	248	361	2081			
23	136	249	362	2194	456	481	784CIP2B_77
24	137	250	363	2613			
25	138	251	364	2628			
26	139	252	365	2633			
27	140	253	366	2677			
28	141	254	367	2845			
29	142	255	368	2845			
30	143	256	369	2921			
31	144	257	370	2983			
32	145	258	371	3003			
33	146	259	372	3217			
34	147	260	373	3448	472	497	784CIP2C_37
34	147	260	373	3448	473	498	784CIP2C_38
35	148	261	374	3489			
36	149	262	375	3534			
37	150	263	376	3657	477	502	784CIP2E_3
38	151	264	377	3744			
39	152	265	378	3896			
40	153	266	379	4062			
41	154	267	380	41			
42	155	268	381	4122			
43	156	269	382	4129			
44	157	270	383	4178			
45	158	271	384	4180			
46	159	272	385	4184			
47	160	273	386	4189			
48	161	274	387	4191			
49	162	275	388	4293			
50	163	276	389	4298			
51	164	277	390	4345			
52	165	278	391	4452			
53	166	279	392	4507			
54	167	280	393	4543			

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SEQ ID NO: OF NUCLEIC ACIDS	SEQ ID NO: OF POLY- PEPTIDE	SEQ ID NO: OF CONTIG NUCLEIC ACIDS	SEQ ID NO: OF CONTIG POLY- PEPTIDE	SEQ ID NO: OF CONTIG IN U.S.S.N. 09/488,725	SEQ ID NO: OF FULL- LENGTH NUCLEIC ACIDS	SEQ ID NO: OF FULL- LENGTH POLY- PEPTIDE	DOCKET NO FULL-LENGTH SEQUENCE_ SEQ ID NO: IN APPLICA- TION
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## CLAIMS

### WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-113, 227-339, and 453-477, a mature protein coding portion of SEQ ID NO: 1-113, 227-339, or 453-477, an active domain coding portion of SEQ ID NO: 1-113, 227-339, or 453-477, and complementary sequences thereof.  
5
2. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions.  
10
3. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 90% sequence identity with the polynucleotide of claim 1.  
15
4. The polynucleotide of claim 1 wherein said polynucleotide is DNA.
5. An isolated polynucleotide of claim 1 wherein said polynucleotide comprises the complementary sequences.  
20
6. A vector comprising the polynucleotide of claim 1.
7. An expression vector comprising the polynucleotide of claim 1.  
25
8. A host cell genetically engineered to comprise the polynucleotide of claim 1.
9. A host cell genetically engineered to comprise the polynucleotide of claim 1 operatively associated with a regulatory sequence that modulates expression of the polynucleotide in the host cell.  
30

10. An isolated polypeptide, wherein the polypeptide is selected from the group consisting of:
- (a) a polypeptide encoded by any one of the polynucleotides of claim 1;
  - (b) a polypeptide encoded by a polynucleotide hybridizing under stringent  
5 conditions with any one of SEQ ID NO: 1-113, 227-339, and 453-477; and
  - (c) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 114 – 226, 340 – 452 and 478-502; the mature protein portion thereof, or the active domain thereof.
- 10 11. A composition comprising the polypeptide of claim 10 and a carrier.
12. An antibody directed against the polypeptide of claim 10.
13. A method for detecting the polynucleotide of claim 1 in a sample, comprising:
- 15 a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide of claim 1 for a period sufficient to form the complex; and
  - b) detecting the complex, so that if a complex is detected, the polynucleotide of claim 1 is detected.
- 20
14. A method for detecting the polynucleotide of claim 1 in a sample, comprising:
- a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the polynucleotide of claim 1 under such conditions;
  - 25 b) amplifying a product comprising at least a portion of the polynucleotide of claim 1; and
  - c) detecting said product and thereby the polynucleotide of claim 1 in the sample.

15. The method of claim 14, wherein the polynucleotide is an RNA molecule and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.
- 5 16. A method for detecting the polypeptide of claim 10 in a sample, comprising:
- a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex; and
  - b) detecting formation of the complex, so that if a complex formation
- 10 is detected, the polypeptide of claim 10 is detected.
17. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:
- a) contacting the compound with the polypeptide of claim 10 under
- 15 conditions sufficient to form a polypeptide/compound complex; and
- b) detecting the complex, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.
18. A method for identifying a compound that binds to the polypeptide of claim 10,
- 20 comprising:
- a) contacting the compound with the polypeptide of claim 10, in a cell, under conditions sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and
  - b) detecting the complex by detecting reporter gene sequence
- 25 expression, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.
19. A method of producing the polypeptide of claim 10, comprising:
- a) culturing a host cell comprising a polynucleotide sequence selected
- 30 from the group consisting of a polynucleotide sequence of SEQ ID NO: 1-113, 227-339, or 453-477, a mature protein coding portion of SEQ ID NO: 1-113, 227-339, or 453-477,

an active domain of SEQ ID NO: 1-113, 227-339, or 453-477, complementary sequences thereof and a polynucleotide sequence hybridizing under stringent conditions to SEQ ID NO: 1-113, 227-339, or 453-477, under conditions sufficient to express the polypeptide in said cell; and

- 5                   b)       isolating the polypeptide from the cell culture or cells of step (a).

20.   The isolated polypeptide of claim 10 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 114-226, 340-452 or 478-502, the mature protein portion thereof, or the active domain thereof.

10

21.   The polypeptide of claim 20 wherein the polypeptide is provided on a polypeptide array.

22.   A collection of polynucleotides, wherein the collection comprising the sequence  
15 information of at least one of SEQ ID NO: 1-113, 227-339, and 453-477.

23.   The collection of claim 22, wherein the collection is provided on a nucleic acid array.

20 24.   The collection of claim 23, wherein the array detects full-matches to any one of the polynucleotides in the collection.

25.   The collection of claim 23, wherein the array detects mismatches to any one of the polynucleotides in the collection.

25

26.   The collection of claim 22, wherein the collection is provided in a computer-readable format.

27.   A method of treatment comprising administering to a mammalian subject in need  
30 thereof a therapeutic amount of a composition comprising a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

28. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising an antibody that specifically binds to a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

5

29. A method of detecting bone marrow cells or tissues in a sample comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide of claim 1 for a period sufficient to form a complex; and

b) detecting the complex, so that if a complex is detected, the polynucleotide of claim 1 is detected

wherein the presence of the polynucleotide of claim 1 indicates the presence of bone marrow cells or tissues.

30. A method for detecting bone marrow cells or tissue in a sample comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form a complex; and

b) detecting formation of the complex so that if a complex is detected, the polypeptide of claim 10 is detected,

wherein the presence of the polypeptide of claim 10 indicates the presence of bone marrow cells or tissues in a sample.

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 <212> DNA  
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&lt;211&gt; 667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

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&lt;211&gt; 1940

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 57

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<212> DNA

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&lt;210&gt; 62

&lt;211&gt; 2271

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2271)

&lt;223&gt; n = a,t,c or g.

&lt;400&gt; 62

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 <212> DNA  
 <213> Homo sapiens

<400> 63						
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 <211> 801  
 <212> DNA  
 <213> Homo sapiens

<220>  
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 <222> (1)...(801)  
 <223> n = a,t,c or g

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&lt;210&gt; 65

&lt;211&gt; 2222

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2222)

&lt;223&gt; n = a,t,c or g

&lt;400&gt; 65

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<210> 66
<211> 1800
<212> DNA
<213> Homo sapiens

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<210> 67
<211> 2081
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (1)...(2081)
<223> n = a,t,c or g

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&lt;210&gt; 68

&lt;211&gt; 3405

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 68

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

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&lt;211&gt; 3622

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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 <212> DNA  
 <213> Homo sapiens

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<210> 112  
 <211> 905  
 <212> DNA  
 <213> Homo sapiens

<400> 112

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&lt;211&gt; 2722

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

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<210> 114  
 <211> 248  
 <212> PRT  
 <213> Homo sapiens

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<400> 114
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Asp Ala Gly Met Ala Glu Ala Arg Val Leu Met Thr Arg Lys Thr Glu
          20          25          30
Ile Ile Val Pro Glu Ala Glu Lys Glu Glu Ala Gln Thr Phe Gly Val
          35          40          45
Gln Glu Ala Glu Thr Arg Val Gly Ser Ala Leu Lys Tyr Glu Ala Leu
          50          55          60
Arg Ala Pro Val Thr Gln Pro Arg Val Leu Gly Ser Gln Glu Ala Lys
          65          70          75          80
Ala Glu Ile Ser Gly Val Gln Gly Ser Glu Thr Gln Val Leu Arg Val
          85          90          95
Gln Glu Ala Glu Ala Gly Val Trp Gly Met Ser Glu Gly Lys Ser Gly
          100          105          110
Ala Trp Gly Ala Gln Glu Ala Glu Met Lys Val Leu Glu Ser Pro Glu
          115          120          125
Asn Lys Ser Gly Thr Phe Lys Ala Gln Glu Ala Glu Ala Gly Gly Leu
          130          135          140
Gly Lys Leu Arg Arg Gly Lys Lys Leu Arg Glu Ala Ser Gln Arg Pro
          145          150          155          160
Ala Cys Leu Lys His Arg Trp Pro Ser Gly Ala Gly Ala Trp Gly Ala
          165          170          175
Gln Gly Leu Phe Pro Arg Glu Gly Leu Lys Arg Thr Gly Gly Leu Pro
          180          185          190
Gly Ser Gln Ala Pro Pro Ala Leu Val Ser Ser Ser Gln Ser Leu Leu
          195          200          205
Glu Trp Cys Gln Glu Val Thr Thr Gly Tyr Arg Gly Val Arg Ile His
          210          215          220
Gln Leu His His Ile Leu Ala Gln Arg Leu Gly Leu Leu Cys His Pro
          225          230          235          240
Ala Pro Ile Leu Pro Arg Gln Asp
          245          248

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<210> 115  
 <211> 148  
 <212> PRT  
 <213> Homo sapiens

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<400> 115
Met Arg Arg Gly Ser Gly Cys Gly Arg Gly Pro Thr Ser Thr Ala Leu

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Cys Trp Arg Ser Ser Thr Ser Ser Asn Ala Leu Ala Asp Ala Lys Gly
      20           25           30
Arg Lys Thr His Val Ser Tyr Arg Asp Ser Lys Leu Ile Arg Val Leu
      35           40           45
Lys Asp Ser Leu Gly Gly Asn Cys Arg Thr Val Met Ile Ala Ala Ile
      50           55           60
Ser Pro Ser Ser Leu Thr Tyr Glu Asp Thr Tyr Asn Thr Leu Lys Tyr
      65           70           75           80
Ala Asp Arg Ala Lys Glu Ile Arg Leu Ser Leu Lys Ser Asn Val Thr
      85           90           95
Ser Leu Asp Cys His Ile Ser Gln Tyr Ala Thr Ile Cys Gln Gln Leu
      100          105          110
Gln Ala Glu Val Ala Ala Leu Arg Lys Lys Leu Gln Val Tyr Glu Gly
      115          120          125
Gly Gly Gln Pro Pro Pro Gln Asp Leu Pro Gly Ser Pro Lys Ser Gly
      130          135          140
Pro Pro Pro Glu
145          148

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<210> 116
<211> 563
<212> PRT
<213> Homo sapiens

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      <400> 116
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      1           5           10           15
Ser Lys Tyr Asn Leu Ile Asn Glu Gly Ser Pro Pro Ser Lys Ile Met
      20           25           30
Lys Ala Val Tyr Gln Asn Ile Ser Glu Ser Asn Pro Ala Tyr Glu Val
      35           40           45
Phe Gln Thr Asp Thr Ile Glu Tyr Gly Glu Ile Leu Ser Phe Pro Glu
      50           55           60
Ser Pro Ser Ile Glu Phe Lys Gln Phe Ser Thr Lys His Ile Gln Gln
      65           70           75           80
Tyr Val Glu Asn Ile Ile Pro Glu Tyr Ile Ser Ala Phe Ala Asn Thr
      85           90           95
Glu Gly Gly Tyr Leu Phe Ile Gly Val Asp Asp Lys Ser Arg Lys Val
      100          105          110
Leu Gly Cys Ala Lys Glu Gln Val Asp Pro Asp Ser Leu Lys Asn Val
      115          120          125
Ile Ala Arg Ala Ile Ser Lys Leu Pro Ile Val His Phe Cys Ser Ser
      130          135          140
Lys Pro Arg Val Glu Tyr Ser Thr Lys Ile Val Glu Val Phe Cys Gly
      145          150          155          160
Lys Glu Leu Tyr Gly Tyr Leu Cys Val Ile Lys Val Lys Ala Phe Cys
      165          170          175
Cys Val Val Phe Ser Glu Ala Pro Lys Ser Trp Met Val Arg Glu Lys
      180          185          190
Tyr Ile Arg Pro Leu Thr Thr Glu Glu Trp Val Glu Lys Met Met Asp
      195          200          205
Ala Asp Pro Glu Phe Pro Pro Asp Phe Ala Glu Ala Phe Glu Ser Gln
      210          215          220
Leu Ser Leu Ser Asp Ser Pro Ser Leu Cys Arg Pro Val Tyr Ser Lys
      225          230          235          240
Lys Gly Leu Glu His Lys Ala Asp Leu Gln Gln His Leu Phe Pro Gly
      245          250          255
Thr Asp Cys Gln Phe Leu His Gln Glu Arg Arg Lys Ser Phe Asn Thr
      260          265          270
Phe Arg Gly Lys Gln Ile His Glu Arg Leu Cys Pro Ala Asp Pro Val

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      275      280      285
Pro Pro Gly His Leu Glu Cys Thr Pro Glu Ser Leu Trp Lys Glu Leu
 290      295      300
Ser Leu Gln His Glu Gly Leu Lys Glu Leu Ile His Lys Gln Met Arg
305      310      315      320
Pro Phe Ser Gln Gly Ile Val Ile Leu Ser Arg Ser Trp Ala Val Asp
      325      330      335
Leu Asn Leu Gln Glu Lys Pro Gly Val Ile Cys Asp Ala Leu Leu Ile
      340      345      350
Ala Gln Asn Ser Thr Pro Ile Leu Tyr Thr Ile Leu Arg Glu Gln Asp
      355      360      365
Ala Glu Gly Gln Asp Tyr Cys Thr Arg Thr Ala Phe Thr Leu Lys Gln
      370      375      380
Lys Leu Val Asn Met Gly Gly Tyr Thr Gly Lys Val Cys Val Arg Ala
385      390      395      400
Lys Val Leu Cys Leu Ser Pro Glu Ser Ser Ala Glu Ala Leu Glu Ala
      405      410      415
Ala Val Ser Pro Met Asp Tyr Pro Ala Ser Tyr Ser Leu Ala Gly Thr
      420      425      430
Gln His Met Glu Ala Leu Leu Gln Ser Leu Val Ile Val Leu Leu Gly
      435      440      445
Phe Arg Ser Leu Leu Ser Asp Gln Leu Gly Cys Glu Val Leu Asn Leu
450      455      460
Leu Thr Ala Gln Gln Tyr Glu Ile Phe Ser Arg Ser Leu Arg Lys Asn
465      470      475      480
Arg Glu Leu Phe Val His Gly Leu Pro Gly Ser Gly Lys Thr Ile Met
      485      490      495
Ala Met Lys Ile Met Glu Lys Ile Arg Asn Val Phe His Cys Glu Ala
      500      505      510
His Arg Ile Leu Tyr Val Cys Glu Asn Gln Pro Leu Arg Asn Phe Ile
      515      520      525
Ser Asp Arg Asn Ile Cys Arg Ala Glu Thr Arg Glu Thr Phe Leu Arg
      530      535      540
Glu Lys Phe Glu His Ile Gln His Ile Val Ile Asp Glu Ala Gln Asn
545      550      555      560
Phe Pro Tyr
      563

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<210> 117
<211> 182
<212> PRT
<213> Homo sapiens

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      <400> 117
Met Met Thr Asp Thr Asp Pro Asp Leu Leu Gln Leu Ser Glu Asp Phe
 1      5      10      15
Glu Cys Gln Leu Ser Leu Ser Ser Gly Pro Pro Leu Ser Arg Pro Val
      20      25      30
Tyr Ser Lys Lys Gly Leu Glu His Lys Lys Glu Leu Gln Gln Leu Leu
      35      40      45
Phe Ser Val Pro Pro Gly Tyr Leu Arg Tyr Thr Pro Glu Ser Leu Trp
      50      55      60
Arg Asp Leu Ile Ser Glu His Arg Gly Leu Glu Glu Leu Ile Asn Lys
      65      70      75      80
Gln Met Gln Pro Phe Phe Arg Gly Ile Leu Ile Phe Ser Arg Ser Trp
      85      90      95
Ala Val Asp Leu Asn Leu Gln Glu Lys Pro Gly Val Ile Cys Asp Ala
      100      105      110
Leu Leu Ile Ala Gln Asn Ser Thr Pro Ile Leu Tyr Thr Ile Leu Arg
      115      120      125
Glu Gln Asp Ala Glu Gly Gln Asp Tyr Cys Thr Cys Thr Ala Phe Thr

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      130              135              140
Leu Lys Gln Lys Leu Val Asn Met Gly Gly Tyr Thr Gly Lys Val Cys
145              150              155              160
Val Arg Ala Lys Val Leu Cys Met Ser Pro Glu Ser Ser Ala Glu Ala
              165              170              175
Leu Glu Ala Ala Val Ser
              180              182

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<210> 118
<211> 49
<212> PRT
<213> Homo sapiens

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      <400> 118
Met Ile Leu Gln Gly Pro Ser Gln Phe Pro Arg Gly Thr Asn Lys Leu
 1              5              10              15
Trp His Gly Gln Leu Leu Arg Ala Thr Gly Ser Ser Leu Pro Val Ser
              20              25              30
Leu Val Leu Gln Gln Pro Ala Ser Trp Ala Leu Gly Cys Glu Pro Asp
              35              40              45
Glu
49

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<210> 119
<211> 163
<212> PRT
<213> Homo sapiens

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```

      <400> 119
Met Ser Pro Pro Thr Val Pro Pro Met Gly Val Asp Gly Val Ser Ala
 1              5              10              15
Tyr Leu Met Lys Lys Arg His Thr His Arg Lys His Arg Arg Lys Pro
              20              25              30
Thr Phe Leu Thr Arg Arg Asn Ile Val Gly Tyr Arg Ile Gln His Gly
              35              40              45
Trp Lys Glu Gly Thr Glu Pro Gly Arg Gln Cys Lys Gly Thr Val Leu
              50              55              60
Glu Gln Val Ser Val Lys Pro Thr Leu Tyr Ile Ile Lys Tyr Asp Gly
 65              70              75              80
Lys Asp Ser Val Tyr Gly Leu Glu Leu Pro Arg His Lys Arg Val Leu
              85              90              95
Ala Leu Glu Ile Leu Pro Glu Arg Val Pro Thr Pro Arg Ile Asp Ser
              100              105              110
Arg Leu Ala Asp Ser Leu Ile Gly Lys Ala Val Glu His Val Phe Glu
              115              120              125
Gly Glu His Gly Thr Lys Asp Glu Trp Lys Gly Met Val Leu Ala Arg
 130              135              140
Ala Pro Val Met Asp Thr Trp Phe Tyr Ile Thr Tyr Glu Lys Asp Pro
145              150              155              160
Val Ser Leu
              163

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<210> 120
<211> 136
<212> PRT
<213> Homo sapiens

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&lt;400&gt; 120

```

Met Gly Gly Met Thr Pro Phe Ile Ser Ala Leu Gln Ser Thr Asp Trp
 1          5          10          15
Leu Cys Asn Gly Glu Leu Ser His Asp Cys Asp Gly Pro Ile Thr Asp
          20          25          30
Leu Asn Ser Asp Gln Tyr Gln Tyr Met Asn Gly Lys Asn Lys His Ser
          35          40          45
Val Arg Arg Leu Asp Pro Glu Tyr Trp Lys Thr Ile Leu Ser Cys Ile
          50          55          60
Tyr Val Phe Ile Val Phe Gly Phe Thr Ser Phe Ile Met Val Ile Val
          65          70          75          80
His Glu Arg Val Pro Asp Met Gln Thr Tyr Pro Pro Leu Pro Asp Ile
          85          90          95
Phe Leu Asp Ser Val Pro Arg Ile Pro Trp Ala Phe Ala Met Thr Glu
          100          105          110
Val Cys Gly Met Ile Leu Cys Tyr Ile Trp Leu Leu Val Phe Phe Ser
          115          120          125
Tyr Lys His Lys Ser Ile Leu Leu
          130          135 136

```

&lt;210&gt; 121

&lt;211&gt; 378

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 121

```

Met Gly Arg Leu Ala Glu Ala Gln Thr Tyr Leu Asp Lys Val Glu Asn
 1          5          10          15
Thr Cys Lys Lys Phe Ala Asn Pro Ser Arg Tyr Arg Met Glu Cys Pro
          20          25          30
Glu Val Asp Cys Glu Glu Gly Trp Ala Leu Ala Lys Cys Gly Gly Lys
          35          40          45
Asn Tyr Glu Arg Ala Lys Thr Cys Phe Glu Lys Ala Leu Glu Gly Asn
          50          55          60
Pro Glu Asn Pro Glu Phe Asn Thr Gly Tyr Ala Ile Thr Val Tyr Arg
          65          70          75          80
Leu Asp Lys Phe Asn Thr Ala Ser Gly Arg Asn Lys Ala Phe Ser Leu
          85          90          95
His Val Leu Lys Arg Ala Val Arg Leu Asn Pro Asp Asp Val Tyr Ile
          100          105          110
Arg Val Leu Leu Ala Leu Lys Leu Gln Asp Glu Gly Gln Glu Ala Glu
          115          120          125
Gly Glu Lys Tyr Ile Glu Glu Ala Leu Thr Ser Ile Ser Ser Gln Ala
          130          135          140
Tyr Val Phe Gln Tyr Ala Ala Lys Phe Tyr Arg Arg Lys Gly Ser Val
          145          150          155          160
Asp Lys Ala Leu Glu Leu Leu Lys Met Ala Leu Glu Thr Thr Pro Thr
          165          170          175
Ser Ala Phe Leu His His Gln Met Gly Leu Cys Tyr Arg Ala Gln Met
          180          185          190
Ile Gln Ile Lys Glu Ala Thr Asn Trp Gln Pro Arg Gly Gln Asp Arg
          195          200          205
Glu Thr Val Asp Arg Leu Val Gln Leu Ala Ile Cys Lys Phe Glu Lys
          210          215          220
Thr Ile Met Leu Lys Arg Thr Phe Glu Met Ala Tyr Val Asp Leu Ala
          225          230          235          240
Glu Thr Tyr Ala Glu Ile Gly His His Arg Lys Ala Glu Glu His Phe
          245          250          255
Gln Lys Gly Leu Arg Met Lys Ile Phe Glu Asp Gln Leu Lys Gln Glu
          260          265          270
Ile His Tyr His Tyr Gly Arg Phe Gln Glu His His Gly Lys Ser Gln

```



```

      275              280              285
Asp Lys Ala Ile Thr His Tyr Leu Lys Gly Leu Lys Ile Glu Lys Met
 290              295              300
Ser His Ser Arg Glu Lys Leu Leu Asn Ala Leu Glu Lys Leu Ala Lys
 305              310              315              320
Arg Cys Ile His Gln Asn Val Arg Val Val Glu Ser Val Ser Leu Leu
      325              330              335
Gly Leu Ile His Lys Leu Lys Gly Glu Cys Gly Gly Ser Val Arg Val
      340              345              350
Val Gly Lys Thr Ile Gly Lys Gly Cys Lys Pro Ser Glu Ser Leu Glu
      355              360              365
Gly Ser Ala Glu Pro Arg Gly Arg Asn Ser
 370              375              378

```

<210> 122  
 <211> 348  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 122
Met Leu Asp Lys Cys Pro Phe Pro Pro Arg Ser Asp Leu Ala Phe Arg
 1              5              10              15
Trp His Phe Ile Lys Arg His Thr Ala Pro Ile Asn Ser Lys Ser Asp
      20              25              30
Glu Trp Val Ser Thr Asp Leu Ser Gln Thr Glu Leu Arg Asp Gly Gln
      35              40              45
Leu Lys Arg Arg Asn Met Glu Glu Asn Ile Asn Cys Phe Ser His Thr
      50              55              60
Asn Val Gln Pro Cys Val Ile Thr Thr Asp Asn Ala Leu Cys Arg Glu
      65              70              75              80
Gly Pro Met Thr Gly Ser Val Met Asn Leu Val Ser Asn Asn Ser Ile
      85              90              95
Glu Asp Ser Asp Met Asp Ser Asp Asp Glu Ile Leu Thr Leu Cys Thr
      100              105              110
Ser Ser Arg Lys Arg Asn Lys Pro Lys Trp Asp Leu Asp Asp Glu Ile
      115              120              125
Leu Gln Leu Glu Thr Pro Pro Lys Tyr His Thr Gln Ile Asp Tyr Val
      130              135              140
His Cys Leu Val Pro Asp Leu Leu Gln Ile Asn Asn Asn Pro Cys Tyr
      145              150              155              160
Trp Gly Val Met Asp Lys Tyr Ala Ala Glu Ala Leu Leu Glu Gly Lys
      165              170              175
Pro Glu Gly Thr Phe Leu Leu Arg Asp Ser Ala Gln Glu Asp Tyr Leu
      180              185              190
Phe Ser Val Ser Phe Arg Arg Tyr Ser Arg Ser Leu His Ala Arg Ile
      195              200              205
Glu Gln Trp Asn His Asn Phe Ser Phe Asp Ala His Asp Pro Cys Val
      210              215              220
Phe His Ser Pro Asp Ile Thr Gly Leu Leu Glu His Tyr Lys Asp Pro
      225              230              235              240
Ser Ala Cys Met Phe Phe Glu Pro Leu Leu Ser Thr Pro Leu Ile Arg
      245              250              255
Thr Phe Pro Phe Ser Leu Gln His Ile Cys Arg Thr Val Ile Cys Asn
      260              265              270
Cys Thr Thr Tyr Asp Gly Ile Asp Ala Leu Pro Ile Pro Ser Ser Met
      275              280              285
Lys Leu Tyr Leu Lys Glu Tyr His Tyr Lys Ser Lys Val Arg Val Leu
      290              295              300
Arg Ile Asp Ala Pro Glu Gln Gln Cys Tyr Cys Arg Gln Ser Gly Cys
      305              310              315              320
Ala Arg Val Phe Arg Ala Gln Ser Leu Gly Pro Ile Ala Ala Ser Arg

```

Pro Tyr Cys Gly Leu Gly Tyr Cys Arg Glu Asn Val  
 340 325 330 335  
 345 348

<210> 123  
 <211> 513  
 <212> PRT  
 <213> Homo sapiens

<400> 123  
 Met Thr Tyr Ser Val Gln Asp His Met Glu Thr Arg Gln Gln Met Ser  
 1 5 10 15  
 Ala Glu Leu Trp Lys Asp Arg Leu Ala Val Leu Lys Glu Glu Asn Asp  
 20 25 30  
 Lys Lys Arg Ala Glu Lys Gln Lys Arg Lys Glu Met Glu Ala Lys Asn  
 35 40 45  
 Lys Glu Asn Gly Lys Val Glu Asn Gly Leu Gly Lys Thr Asp Arg Lys  
 50 55 60  
 Lys Glu Ile Val Lys Phe Glu Pro Gln Val Asp Thr Glu Ala Glu Asp  
 65 70 75 80  
 Met Ile Ser Ala Val Lys Ser Arg Arg Leu Ala Ile Gln Ala Lys  
 85 90 95  
 Lys Glu Arg Glu Ile Gln Glu Arg Glu Met Lys Glu Leu Ser Gly Leu  
 100 105 110  
 Phe Cys Pro Tyr Arg Phe Leu Cys Asp Ser Gln Lys Glu Leu Asp Glu  
 115 120 125  
 Leu Leu Asn Cys Leu His Pro Gln Gly Ile Arg Glu Ser Gln Leu Lys  
 130 135 140  
 Glu Arg Leu Glu Lys Arg Tyr Gln Asp Ile Ile His Ser Ile His Leu  
 145 150 155 160  
 Ala Arg Lys Pro Asn Leu Gly Leu Lys Ser Cys Asp Gly Asn Gln Glu  
 165 170 175  
 Leu Leu Asn Phe Leu Arg Ser Asp Leu Ile Glu Val Ala Thr Arg Leu  
 180 185 190  
 Gln Lys Gly Gly Leu Gly Tyr Val Glu Glu Thr Ser Glu Phe Glu Ala  
 195 200 205  
 Arg Val Ala Ser Ala Leu Glu Lys Trp Lys Thr Ala Ile Arg Glu Ala  
 210 215 220  
 Gln Thr Phe Ser Arg Met His Val Leu Leu Gly Met Leu Asp Ala Cys  
 225 230 235 240  
 Ile Lys Trp Asp Met Ser Ala Glu Asn Ala Arg Cys Lys Val Cys Arg  
 245 250 255  
 Lys Lys Gly Glu Asp Asp Lys Leu Ile Leu Cys Asp Glu Cys Asn Lys  
 260 265 270  
 Ala Phe His Leu Phe Cys Leu Arg Pro Ala Leu Tyr Glu Val Pro Asp  
 275 280 285  
 Val Arg Pro Arg Lys Thr Ile Arg Gly Lys His Ser Val Ile Pro Pro  
 290 295 300  
 Ala Ala Arg Ser Gly Arg Arg Pro Gly Lys Lys Pro His Ser Thr Arg  
 305 310 315 320  
 Arg Ser Gln Pro Lys Ala Pro Pro Val Asp Asp Ala Glu Val Asp Glu  
 325 330 335  
 Leu Val Leu Gln Thr Lys Arg Ser Ser Arg Arg Gln Ser Leu Glu Leu  
 340 345 350  
 Gln Lys Cys Glu Glu Ile Leu His Lys Ile Val Lys Tyr Arg Phe Ser  
 355 360 365  
 Trp Pro Phe Arg Thr Cys Leu Ser Gly Arg Gly Thr Ala Val Lys Ala  
 370 375 380  
 Val Gln Ile Leu His Leu Val Leu Leu His Arg Glu Pro Val Thr Arg  
 385 390 395 400  
 Asp Glu Ala Glu Asp Tyr Tyr Asp Val Ile Thr His Pro Met Asp Phe

405 410 415  
 Gln Thr Val Gln Asn Lys Cys Ser Cys Gly Ser Tyr Arg Ser Val Gln  
 420 425 430  
 Glu Phe Leu Thr Asp Met Lys Gln Val Phe Thr Asn Ala Glu Val Tyr  
 435 440 445  
 Asn Cys Arg Gly Ser His Val Leu Ser Cys Met Val Lys Thr Glu Gln  
 450 455 460  
 Cys Leu Val Ala Leu Leu His Lys His Leu Pro Gly His Pro Tyr Val  
 465 470 475 480  
 Arg Arg Lys Arg Lys Lys Phe Pro Asp Arg Leu Ala Glu Asp Glu Gly  
 485 490 495  
 Asp Ser Glu Pro Glu Ala Val Gly Gln Ser Arg Gly Arg Arg Gln Lys  
 500 505 510  
 Lys  
 513

<210> 124  
 <211> 1302  
 <212> PRT  
 <213> Homo sapiens

<400> 124  
 Met Glu Glu Leu Ser Ala Asp Glu Ile Arg Arg Arg Arg Leu Ala Arg  
 1 5 10 15  
 Leu Ala Gly Gly Gln Thr Ser Gln Pro Thr Thr Pro Leu Thr Ser Pro  
 20 25 30  
 Gln Arg Glu Asn Pro Pro Gly Pro Pro Ile Ala Ala Ser Ala Pro Gly  
 35 40 45  
 Pro Ser Gln Ser Leu Gly Leu Asn Val His Asn Met Thr Pro Ala Thr  
 50 55 60  
 Ser Pro Ile Gly Ala Ser Gly Val Ala His Arg Ser Gln Ser Ser Glu  
 65 70 75 80  
 Gly Val Ser Ser Leu Ser Ser Ser Pro Ser Asn Ser Leu Glu Thr Gln  
 85 90 95  
 Ser Gln Ser Leu Ser Arg Ser Gln Ser Met Asp Ile Asp Gly Val Ser  
 100 105 110  
 Cys Glu Lys Ser Met Ser Gln Val Asp Val Asp Ser Gly Ile Glu Asn  
 115 120 125  
 Met Glu Val Asp Glu Asn Asp Arg Arg Glu Lys Arg Ser Leu Ser Asp  
 130 135 140  
 Lys Glu Pro Ser Ser Gly Pro Glu Val Ser Glu Glu Gln Ala Leu Gln  
 145 150 155 160  
 Leu Val Cys Lys Ile Phe Arg Val Ser Trp Lys Asp Arg Asp Arg Asp  
 165 170 175  
 Val Ile Phe Leu Ser Ser Leu Ser Ala Gln Phe Lys Gln Asn Pro Lys  
 180 185 190  
 Glu Val Phe Ser Asp Phe Lys Asp Leu Ile Gly Gln Ile Leu Met Glu  
 195 200 205  
 Val Leu Met Met Ser Thr Gln Thr Arg Asp Glu Asn Pro Phe Ala Ser  
 210 215 220  
 Leu Thr Ala Thr Ser Gln Pro Ile Ala Ala Ala Arg Ser Pro Asp  
 225 230 235 240  
 Arg Asn Leu Leu Leu Asn Thr Gly Ser Asn Pro Gly Thr Ser Pro Met  
 245 250 255  
 Phe Cys Ser Val Ala Ser Phe Gly Ala Ser Ser Leu Ser Ser Leu Tyr  
 260 265 270  
 Glu Ser Ser Pro Ala Pro Thr Pro Ser Phe Trp Ser Ser Val Pro Val  
 275 280 285  
 Met Gly Pro Ser Leu Ala Ser Pro Ser Arg Ala Ala Ser Gln Leu Ala  
 290 295 300  
 Val Pro Ser Thr Pro Leu Ser Pro His Ser Ala Ala Ser Gly Thr Ala

305					310					315				320	
Ala	Gly	Ser	Gln	Pro	Ser	Ser	Pro	Arg	Tyr	Arg	Pro	Tyr	Thr	Val	Thr
				325					330					335	
His	Pro	Trp	Ala	Ser	Ser	Gly	Val	Ser	Ile	Leu	Ser	Ser	Ser	Pro	Ser
			340					345						350	
Pro	Pro	Ala	Leu	Ala	Ser	Ser	Pro	Gln	Ala	Val	Pro	Ala	Ser	Ser	Ser
		355					360					365			
Arg	Gln	Arg	Pro	Ser	Ser	Thr	Gly	Pro	Pro	Leu	Pro	Pro	Ala	Ser	Pro
	370					375					380				
Ser	Ala	Thr	Ser	Arg	Arg	Pro	Ser	Ser	Leu	Arg	Ile	Ser	Pro	Ser	Leu
385					390					395					400
Gly	Ala	Ser	Gly	Gly	Ala	Ser	Asn	Trp	Asp	Ser	Tyr	Ser	Asp	His	Phe
			405						410					415	
Thr	Ile	Glu	Thr	Cys	Lys	Glu	Thr	Asp	Met	Leu	Asn	Tyr	Leu	Ile	Glu
			420					425					430		
Cys	Phe	Asp	Arg	Val	Gly	Ile	Glu	Glu	Lys	Lys	Ala	Pro	Lys	Met	Cys
	435						440					445			
Ser	Gln	Pro	Ala	Val	Ser	Gln	Leu	Leu	Ser	Asn	Ile	Arg	Ser	Gln	Cys
	450					455					460				
Ile	Ser	His	Thr	Ala	Leu	Val	Leu	Gln	Gly	Ser	Leu	Thr	Gln	Pro	Arg
465					470					475					480
Ser	Leu	Gln	Gln	Pro	Ser	Phe	Leu	Val	Pro	Tyr	Met	Leu	Cys	Arg	Asn
			485						490					495	
Leu	Pro	Tyr	Gly	Phe	Ile	Gln	Glu	Leu	Val	Arg	Thr	Thr	His	Gln	Asp
			500					505					510		
Glu	Glu	Val	Phe	Lys	Gln	Ile	Phe	Ile	Pro	Ile	Leu	Gln	Gly	Leu	Ala
	515						520					525			
Leu	Ala	Ala	Lys	Glu	Cys	Ser	Leu	Asp	Ser	Asp	Tyr	Phe	Lys	Tyr	Pro
	530					535					540				
Leu	Met	Ala	Leu	Gly	Glu	Leu	Cys	Glu	Thr	Lys	Phe	Gly	Lys	Thr	His
545					550					555					560
Pro	Val	Cys	Asn	Leu	Val	Ala	Ser	Leu	Arg	Leu	Trp	Leu	Pro	Lys	Ser
			565						570					575	
Leu	Ser	Pro	Gly	Cys	Gly	Arg	Glu	Leu	Gln	Arg	Leu	Ser	Tyr	Leu	Gly
			580					585					590		
Ala	Phe	Phe	Ser	Phe	Ser	Val	Phe	Ala	Glu	Asp	Asp	Val	Lys	Val	Val
		595					600					605			
Glu	Lys	Tyr	Phe	Ser	Gly	Pro	Ala	Ile	Thr	Leu	Glu	Asn	Thr	Arg	Val
	610					615					620				
Val	Ser	Gln	Ser	Leu	Gln	His	Tyr	Leu	Glu	Leu	Gly	Arg	Gln	Glu	Leu
625					630					635					640
Phe	Lys	Ile	Leu	His	Ser	Ile	Leu	Leu	Asn	Gly	Glu	Thr	Arg	Glu	Ala
			645						650					655	
Ala	Leu	Ser	Tyr	Met	Ala	Ala	Val	Val	Asn	Ala	Asn	Met	Lys	Lys	Ala
			660						665				670		
Gln	Met	Gln	Thr	Asp	Asp	Arg	Leu	Val	Ser	Thr	Asp	Gly	Phe	Met	Leu
	675						680					685			
Asn	Phe	Leu	Trp	Val	Leu	Gln	Gln	Leu	Ser	Thr	Lys	Ile	Lys	Leu	Glu
	690					695					700				
Thr	Val	Asp	Pro	Thr	Tyr	Ile	Phe	His	Pro	Arg	Cys	Arg	Ile	Thr	Leu
705					710					715					720
Pro	Asn	Asp	Glu	Thr	Arg	Val	Asn	Ala	Thr	Met	Glu	Asp	Val	Asn	Asp
			725						730					735	
Trp	Leu	Thr	Glu	Leu	Tyr	Gly	Asp	Gln	Pro	Pro	Phe	Ser	Glu	Pro	Lys
			740					745					750		
Phe	Pro	Thr	Glu	Cys	Phe	Phe	Leu	Thr	Leu	His	Ala	His	His	Leu	Ser
		755					760				765				
Ile	Leu	Pro	Ser	Cys	Arg	Arg	Tyr	Ile	Arg	Arg	Leu	Arg	Ala	Ile	Arg
	770					775					780				
Glu	Leu	Asn	Arg	Thr	Val	Glu	Asp	Leu	Lys	Asn	Asn	Glu	Ser	Gln	Trp
785					790					795					800
Lys	Asp	Ser	Pro	Leu	Ala	Thr	Arg	His	Arg	Glu	Met	Leu	Lys	Arg	Cys
			805						810				815		

Lys Thr Gln Leu Lys Lys Leu Val Arg Cys Lys Ala Cys Ala Asp Ala  
 820 825 830  
 Gly Leu Leu Asp Glu Ser Phe Leu Arg Arg Cys Leu Asn Phe Tyr Gly  
 835 840 845  
 Leu Leu Ile Gln Leu Leu Leu Arg Ile Leu Asp Pro Ala Tyr Pro Asp  
 850 855 860  
 Ile Thr Leu Pro Leu Asn Ser Asp Val Pro Lys Val Phe Ala Ala Leu  
 865 870 875 880  
 Pro Glu Phe Tyr Val Glu Asp Val Ala Glu Phe Leu Phe Phe Ile Val  
 885 890 895  
 Gln Tyr Ser Pro Gln Ala Leu Tyr Glu Pro Cys Thr Gln Asp Ile Val  
 900 905 910  
 Met Phe Leu Val Val Met Leu Cys Asn Gln Asn Tyr Ile Arg Asn Pro  
 915 920 925  
 Tyr Leu Val Ala Lys Leu Val Glu Val Met Phe Met Thr Asn Pro Ala  
 930 935 940  
 Val Gln Pro Arg Thr Gln Lys Phe Phe Glu Met Ile Glu Asn His Pro  
 945 950 955 960  
 Leu Ser Thr Lys Leu Leu Val Pro Ser Leu Met Lys Phe Tyr Thr Asp  
 965 970 975  
 Val Glu His Thr Gly Ala Thr Ser Glu Phe Tyr Asp Lys Phe Thr Ile  
 980 985 990  
 Arg Tyr His Ile Ser Thr Ile Phe Lys Ser Leu Trp Gln Asn Ile Ala  
 995 1000 1005  
 His His Gly Thr Phe Met Glu Glu Phe Asn Ser Gly Lys Gln Phe Val  
 1010 1015 1020  
 Arg Tyr Ile Asn Met Leu Ile Asn Asp Thr Thr Phe Leu Leu Asp Glu  
 1025 1030 1035 1040  
 Ser Leu Glu Ser Leu Lys Arg Ile His Glu Val Gln Glu Met Lys  
 1045 1050 1055  
 Asn Lys Glu Gln Trp Asp Gln Leu Pro Arg Asp Gln Gln Gln Ala Arg  
 1060 1065 1070  
 Gln Ser Gln Leu Ala Gln Asp Glu Arg Val Ser Arg Ser Tyr Leu Ala  
 1075 1080 1085  
 Leu Ala Thr Glu Thr Val Asp Met Phe His Ile Leu Thr Lys Gln Val  
 1090 1095 1100  
 Gln Lys Pro Phe Leu Arg Pro Glu Leu Gly Pro Arg Leu Ala Ala Met  
 1105 1110 1115 1120  
 Leu Asn Phe Asn Leu Gln Gln Leu Cys Gly Pro Lys Cys Arg Asp Leu  
 1125 1130 1135  
 Lys Val Glu Asn Pro Glu Lys Tyr Gly Phe Glu Pro Lys Lys Leu Leu  
 1140 1145 1150  
 Asp Gln Leu Thr Asp Ile Tyr Leu Gln Leu Asp Cys Ala Arg Phe Ala  
 1155 1160 1165  
 Lys Ala Ile Ala Asp Asp Gln Arg Ser Tyr Ser Lys Glu Leu Phe Glu  
 1170 1175 1180  
 Glu Val Ile Ser Lys Met Arg Lys Ala Gly Ile Lys Ser Thr Ile Ala  
 1185 1190 1195 1200  
 Ile Glu Lys Phe Lys Leu Leu Ala Glu Lys Val Glu Glu Ile Val Ala  
 1205 1210 1215  
 Lys Asn Ala Arg Ala Glu Ile Asp Tyr Ser Asp Ala Pro Asp Glu Phe  
 1220 1225 1230  
 Arg Asp Pro Leu Met Asp Thr Leu Met Thr Asp Pro Val Arg Leu Pro  
 1235 1240 1245  
 Ser Gly Thr Ile Met Asp Arg Ser Ile Ile Leu Arg His Leu Leu Asn  
 1250 1255 1260  
 Ser Pro Thr Asp Pro Phe Asn Arg Gln Thr Leu Thr Glu Ser Met Leu  
 1265 1270 1275 1280  
 Glu Pro Val Pro Glu Leu Lys Glu Gln Ile Gln Ala Trp Met Arg Glu  
 1285 1290 1295  
 Lys Gln Asn Ser Asp His  
 1300 1302

<210> 125  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 125  
 Met Gly Arg Trp Ala Met Ala Gly Glu Asp Gly Lys Val Gly Cys Gly  
 1 5 10 15  
 Lys  
 17

<210> 126  
 <211> 209  
 <212> PRT  
 <213> Homo sapiens

<400> 126  
 Met Lys Ile Ala Ser Arg Ser Phe Gln Ile Leu Gly Lys Val Tyr Ser  
 1 5 10 15  
 Val Leu Ser Asp Arg Glu Gln Arg Ala Val Tyr Asp Glu Gln Gly Thr  
 20 25 30  
 Val Asp Glu Asp Ser Pro Val Leu Thr Gln Asp Arg Asp Trp Glu Ala  
 35 40 45  
 Tyr Trp Arg Leu Leu Phe Lys Lys Ile Ser Leu Glu Asp Ile Gln Ala  
 50 55 60  
 Phe Glu Lys Thr Tyr Lys Gly Ser Glu Glu Glu Leu Ala Asp Ile Lys  
 65 70 75 80  
 Gln Ala Tyr Leu Asp Phe Lys Gly Asp Met Asp Gln Ile Met Glu Ser  
 85 90 95  
 Val Leu Cys Val Gln Tyr Thr Glu Glu Pro Arg Ile Arg Asn Ile Ile  
 100 105 110  
 Gln Gln Ala Ile Asp Ala Gly Glu Val Pro Ser Tyr Asn Ala Phe Val  
 115 120 125  
 Lys Glu Ser Thr Gln Lys Met Asn Ala Lys Lys Arg Arg Ala Gln Glu  
 130 135 140  
 Glu Ala Lys Glu Ala Glu Met Ser Arg Lys Glu Leu Gly Leu Asp Glu  
 145 150 155 160  
 Gly Val Asp Ser Leu Lys Ala Ala Ile Gln Ser Arg Gln Lys Asp Trp  
 165 170 175  
 Gln Lys Glu Met Asp Asn Phe Leu Ala Gln Met Glu Ala Lys Tyr Cys  
 180 185 190  
 Lys Ser Ser Lys Gly Gly Gly Lys Lys Ser Ala Leu Lys Lys Lys Lys  
 195 200 205  
 Lys  
 209

<210> 127  
 <211> 177  
 <212> PRT  
 <213> Homo sapiens

<400> 127  
 Met Phe Ile Asn Leu Pro Arg Val Lys Glu Leu Leu Glu Asp Asp Lys  
 1 5 10 15  
 Glu Lys Phe Asn Ile Pro Glu Asp Ser Thr Pro Phe Cys Leu Pro Asn  
 20 25 30  
 Gly Ala Leu Val Trp Thr Phe Leu Lys Pro Ile Leu His Gly Lys Ile

```

      35      40      45
Leu Tyr Thr Pro Asn Thr Pro Glu Ile Asn Thr Val Ile Gln Lys Ala
  50      55      60
Asn Tyr Thr Phe Tyr Ile Val Asp Lys Leu Lys Thr Leu Ser Glu Thr
  65      70      75      80
Leu Leu Glu Met Ser Ser Leu Phe Gln Arg Ser Gly Ser Gly Gln Met
      85      90      95
Phe Asn Gln Leu Gln Glu Ala Leu Arg Asn Lys Phe Val Arg Asn Phe
      100      105      110
Val Glu Asn Gln Leu His Ile Asp Val Asp Lys Leu Thr Glu Lys Leu
      115      120      125
Gln Thr Tyr Gly Gly Leu Leu Asp Glu Met Phe Asn His Ala Gly Ala
      130      135      140
Gly Arg Phe Arg Phe Leu Gly Ser Ile Leu Val Asn Leu Ser Ser Cys
      145      150      155      160
Val Ala Leu Asn Arg Phe Gln Ala Leu Gln Ser Gly Asp Ile Pro Gly
      165      170      175
Lys
177

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<210> 128
<211> 256
<212> PRT
<213> Homo sapiens

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```

      <400> 128
Met Thr Gly Ser Thr Phe Ser Lys Thr Ile Val Lys Gly Ala Lys Arg
  1      5      10      15
Ala Gly Lys Met Thr Ile Gly Arg Gln Tyr Leu Leu Lys Lys Lys Thr
      20      25      30
Gly Thr Ile Val Glu Glu Arg Val Asn Arg Pro Gly Trp Asn Glu Asp
      35      40      45
Asp Asp Val Ser Val Ser Asp Glu Ser Glu Leu Pro Thr Ser Thr Thr
      50      55      60
Leu Lys Ala Ser Glu Lys Ser Thr Met Glu Gln Leu Val Glu Lys Ala
      65      70      75      80
Cys Phe Arg Asp Tyr Gln Arg Leu Gly Leu Gly Thr Ile Ser Gly Ser
      85      90      95
Ser Ser Arg Ser Arg Pro Glu Tyr Phe Arg Ile Thr Ala Ser Asn Arg
      100      105      110
Met Tyr Ser Leu Cys Arg Ser Tyr Pro Gly Leu Leu Val Val Pro Gln
      115      120      125
Ala Val Gln Asp Ser Ser Leu Pro Arg Val Ala Arg Cys Tyr Arg His
      130      135      140
Asn Arg Leu Pro Val Val Cys Trp Lys Asn Ser Arg Ser Gly Thr Leu
      145      150      155      160
Leu Leu Arg Ser Gly Phe His Gly Lys Gly Val Val Gly Leu Phe
      165      170      175
Lys Ser Gln Asn Ser Pro Gln Ala Ala Leu His Leu Pro Asn Ser Leu
      180      185      190
Asn Leu His Pro Gln Asn Phe Lys Val Glu Phe Ala Leu Asn Cys Glu
      195      200      205
Phe Val Pro Val Glu Phe His Glu Ile Arg Gln Val Lys Ala Ser Phe
      210      215      220
Lys Lys Leu Met Arg Ala Cys Ile Pro Ser Thr Ile Pro Thr Asp Ser
      225      230      235      240
Glu Val Thr Phe Leu Lys Ala Leu Gly Asp Ser Glu Trp Phe Pro Gln
      245      250      255      256

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<210> 129  
 <211> 521  
 <212> PRT  
 <213> Homo sapiens

<400> 129  
 Met Ser Val Val His Gln Leu Ser Ala Gly Trp Leu Leu Asp His Leu  
 1 5 10 15  
 Ser Phe Ile Asn Lys Ile Asn Tyr Gln Leu His Gln His His Glu Pro  
 20 25 30  
 Cys Cys Arg Lys Lys Glu Phe Thr Thr Ser Val His Phe Glu Ser Leu  
 35 40 45  
 Gln Met Asp Ser Val Ser Ser Gly Val Cys Ala Ala Phe Ile Ala  
 50 55 60  
 Ser Asp Ser Ser Thr Lys Pro Glu Asn Asp Asp Gly Gly Asn Tyr Glu  
 65 70 75 80  
 Met Phe Thr Arg Lys Phe Val Phe Arg Pro Glu Leu Phe Asp Val Thr  
 85 90 95  
 Lys Pro Tyr Ile Thr Pro Ala Val His Lys Glu Cys Gln Gln Ser Asn  
 100 105 110  
 Glu Lys Glu Asp Leu Met Asn Gly Val Lys Lys Glu Ile Ser Ile Ser  
 115 120 125  
 Ile Ile Gly Lys Lys Arg Lys Arg Cys Val Val Phe Asn Gln Gly Glu  
 130 135 140  
 Leu Asp Ala Met Glu Tyr His Thr Lys Ile Arg Glu Leu Ile Leu Asp  
 145 150 155 160  
 Gly Ser Leu Gln Leu Ile Gln Glu Gly Leu Lys Ser Gly Phe Leu Tyr  
 165 170 175  
 Pro Leu Phe Glu Lys Gln Asp Lys Gly Ser Lys Pro Ile Thr Leu Pro  
 180 185 190  
 Leu Asp Ala Cys Ser Leu Ser Glu Leu Cys Glu Met Ala Lys His Leu  
 195 200 205  
 Pro Ser Leu Asn Glu Met Glu His Gln Thr Leu Gln Leu Val Glu Glu  
 210 215 220  
 Asp Thr Ser Val Thr Glu Gln Asp Leu Phe Leu Arg Val Val Glu Asn  
 225 230 235 240  
 Asn Ser Ser Phe Thr Lys Val Ile Thr Leu Met Gly Gln Lys Tyr Leu  
 245 250 255  
 Leu Pro Pro Lys Ser Ser Phe Leu Leu Ser Asp Ile Ser Cys Met Gln  
 260 265 270  
 Pro Leu Leu Asn Tyr Arg Lys Thr Phe Asp Val Ile Val Ile Asp Pro  
 275 280 285  
 Pro Trp Gln Asn Lys Ser Val Lys Arg Ser Asn Arg Tyr Ser Tyr Leu  
 290 295 300  
 Ser Pro Leu Gln Ile Lys Gln Ile Pro Ile Pro Lys Leu Ala Ala Pro  
 305 310 315 320  
 Asn Cys Leu Leu Val Thr Trp Val Thr Asn Arg Gln Lys His Leu Arg  
 325 330 335  
 Phe Ile Lys Glu Glu Leu Tyr Pro Ser Trp Ser Val Glu Val Val Ala  
 340 345 350  
 Glu Trp His Trp Val Lys Ile Thr Asn Ser Gly Glu Phe Val Phe Pro  
 355 360 365  
 Leu Asp Ser Pro His Lys Lys Pro Tyr Glu Gly Leu Ile Leu Gly Arg  
 370 375 380  
 Val Gln Glu Lys Thr Ala Leu Pro Leu Arg Asn Ala Asp Val Asn Val  
 385 390 395 400  
 Leu Pro Ile Pro Asp His Lys Leu Ile Val Ser Val Pro Cys Thr Leu  
 405 410 415  
 His Ser His Lys Pro Pro Leu Ala Glu Val Leu Lys Asp Tyr Ile Lys  
 420 425 430  
 Pro Asp Gly Glu Tyr Leu Glu Leu Phe Ala Arg Asn Leu Gln Pro Gly



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      435              440              445
Trp Thr Ser Trp Gly Asn Glu Val Leu Lys Phe Gln His Val Asp Tyr
      450              455              460
Phe Ile Ala Leu Glu Ser Gly Ser Trp Thr Met Ile Leu Ile Lys Val
465              470              475              480
Val Val Ser Ser Leu Phe Pro Leu His Phe Ser Leu Asn Tyr Lys Ser
      485              490              495
Phe Phe Ile Cys Cys Tyr Arg Pro Ile Phe Leu Glu Tyr Lys Gln Asp
      500              505              510
Leu Phe Phe Ser Val Arg Asp Gln Lys
      515              520 521

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```

<210> 130
<211> 622
<212> PRT
<213> Homo sapiens

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```

      <400> 130
Met Gly Ala Glu Gly Ala Ala Gly Gly Ala Thr Val Gly Tyr Glu Asp
  1              5              10              15
Asp Ile Ser His Leu Val Gly Ser Gly Ser Gly Ile Lys Ser Thr Gly
      20              25              30
Gln His Gly Thr Ile Arg Asp Trp Gly Thr Asp Gly Glu Asn Leu Ile
      35              40              45
Asn His Arg Thr Ser Arg Glu Leu Ala Ser Thr Leu Ser His Gly Lys
      50              55              60
Ile Pro Pro Gln Ser Ser Gln Pro Cys Thr Thr His Val Glu Thr Cys
      65              70              75              80
Gly Arg Ile Ser Pro His Ser Pro Gln Ala Gly Val Leu Ser Arg His
      85              90              95
Ser Val Cys Arg Phe Cys Pro Ala Arg Gln Pro Gly Glu Gly Asp
      100              105              110
Gln Lys Pro Pro Gln Trp Ala Glu Leu Ala Lys Ile Met Arg Thr Arg
      115              120              125
Ala Lys Glu Ile Glu Val Lys Leu Leu Leu Phe Ala Ile Gln Arg Thr
      130              135              140
Thr Asn Phe Glu Gly Phe Leu Ala Lys Arg Phe Ser Gly Cys Thr Leu
      145              150              155              160
Thr Asp Gly Thr Leu Lys Lys Leu Glu Ser Pro Pro Ser Thr Asn
      165              170              175
Pro Phe Leu Glu Asp Glu Pro Thr Pro Glu Met Glu Glu Leu Ala Thr
      180              185              190
Glu Lys Gly Asp Leu Asp Gln Pro Lys Lys Pro Lys Ala Pro Asp Asn
      195              200              205
Pro Phe His Gly Ile Val Ser Lys Cys Phe Glu Pro His Leu Tyr Val
      210              215              220
Tyr Ile Glu Ser Gln Asp Lys Asn Leu Gly Glu Leu Ile Asp Arg Phe
      225              230              235              240
Val Ala Asp Phe Lys Ala Gln Gly Pro Pro Lys Pro Asn Thr Asp Glu
      245              250              255
Gly Gly Ala Val Leu Pro Ser Cys Ala Asp Leu Phe Val Tyr Tyr Lys
      260              265              270
Lys Cys Met Val Gln Cys Ser Gln Leu Ser Thr Gly Glu Pro Met Ile
      275              280              285
Ala Leu Thr Thr Ile Phe Gln Lys Tyr Leu Arg Glu Tyr Ala Trp Lys
      290              295              300
Ile Leu Ser Gly Asn Leu Pro Lys Thr Thr Thr Ser Ser Gly Gly Leu
      305              310              315              320
Thr Ile Ser Ser Leu Leu Lys Glu Lys Glu Gly Ser Glu Val Ala Lys
      325              330              335
Phe Thr Leu Glu Glu Leu Cys Leu Ile Cys Asn Ile Leu Ser Thr Ala

```

```

      340      345      350
Glu Tyr Cys Leu Ala Thr Thr Gln Gln Leu Glu Glu Lys Leu Lys Glu
      355      360      365
Lys Val Asp Val Ser Leu Ile Glu Arg Ile Asn Leu Thr Gly Glu Met
      370      375      380
Asp Thr Phe Ser Thr Val Ile Ser Ser Ser Ile Gln Leu Leu Val Gln
      385      390      395      400
Asp Leu Asp Ala Ala Cys Asp Pro Ala Leu Thr Ala Met Ser Lys Met
      405      410      415
Gln Trp Gln Asn Val Glu His Val Gly Asp Gln Ser Pro Tyr Val Thr
      420      425      430
Ser Val Ile Leu His Ile Lys Gln Asn Val Pro Ile Ile Arg Asp Asn
      435      440      445
Leu Ala Ser Thr Arg Lys Tyr Phe Thr Gln Phe Cys Val Lys Phe Ala
      450      455      460
Asn Ser Phe Ile Pro Lys Phe Ile Thr His Leu Phe Lys Cys Lys Pro
      465      470      475      480
Ile Ser Met Val Gly Ala Glu Gln Leu Leu Leu Asp Thr His Ser Leu
      485      490      495
Lys Met Val Leu Leu Asp Leu Pro Ser Ile Ser Ser Glu Gly Gly Glu
      500      505      510
Glu Gly Thr Arg Gln Leu His Gln Asp Arg Trp Ser Lys Gly Met Thr
      515      520      525
Arg Ala Glu Met Ile Leu Lys Val Val Met Ala Pro His Glu Pro Leu
      530      535      540
Val Val Phe Val Asp Asn Tyr Ile Lys Leu Leu Thr Asp Cys Asn Thr
      545      550      555      560
Glu Thr Phe Gln Lys Ile Leu Asp Met Lys Gly Leu Lys Arg Ser Glu
      565      570      575
Gln Ser Ser Met Leu Glu Leu Leu Arg Gln Arg Leu Pro Ala Leu Ala
      580      585      590
Leu Gly Gly Arg Lys Leu Arg Leu Thr Val Pro Asp Gly Ala Asn Thr
      595      600      605
Arg Ala Arg Val Val Thr His Pro Gln Ala Arg Glu Thr His
      610      615      620      622

```

<210> 131  
 <211> 231  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 131
Met Leu Gln Gln Val Asn Gly His Asn Pro Gly Ser Asp Gly Gln Ala
  1      5      10      15
Arg Glu Tyr Leu Arg Glu Asp Leu Gln Glu Phe Leu Gly Gly Glu Val
      20      25      30
Leu Leu Tyr Lys Leu Asp Asp Leu Thr Arg Val Asn Pro Val Thr Leu
      35      40      45
Glu Thr Val Leu Arg Cys Leu Gln Ala Arg Tyr Met Ala Asp Thr Phe
      50      55      60
Tyr Thr Asn Ala Gly Cys Thr Leu Val Ala Leu Asn Pro Phe Lys Pro
      65      70      75      80
Val Pro Gln Leu Tyr Ser Pro Glu Leu Met Arg Glu Tyr His Ala Ala
      85      90      95
Pro Gln Pro Gln Lys Leu Lys Pro His Val Phe Thr Val Gly Glu Gln
      100      105      110
Thr Tyr Arg Asn Val Lys Ser Leu Ile Glu Pro Val Asn Gln Ser Ile
      115      120      125
Val Val Ser Gly Glu Ser Gly Ala Gly Lys Thr Trp Thr Ser Arg Cys
      130      135      140
Leu Met Lys Phe Tyr Ala Val Val Ala Thr Ser Pro Ala Ser Trp Glu

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145          150          155          160
Ser His Lys Ile Ala Glu Arg Ile Glu Gln Arg Ile Leu Asn Ser Asn
          165          170          175
Pro Val Met Glu Ala Phe Gly Asn Ala Cys Thr Leu Arg Asn Asn Asn
          180          185          190
Ser Ser Arg Phe Gly Lys Val His Gln Ala Gln Ala Glu Gln Gly Ser
          195          200          205
Ala Asn Asp Trp Ser Arg Ser Pro Asp Leu Pro Pro Arg Glu Asn Ser
          210          215          220
Ser Gly Leu Pro Gly Phe Gln
225          230 231

```

<210> 132  
 <211> 246  
 <212> PRT  
 <213> Homo sapiens

```

<400> 132
Met Phe Ser Glu Glu Cys Ile Met Asp Val Ile Gly Cys Leu Glu Tyr
 1          5          10          15
Asp Pro Ala Leu Ser Gln Pro Arg Lys His Arg Glu Phe Leu Thr Lys
          20          25          30
Thr Ala Lys Phe Lys Glu Val Ile Pro Ile Ser Asp Pro Glu Leu Lys
          35          40          45
Gln Lys Ile His Gln Thr Tyr Arg Val Gln Tyr Ile Gln Asp Met Val
          50          55          60
Leu Pro Thr Pro Ser Val Phe Glu Glu Asn Met Leu Ser Thr Leu His
          65          70          75          80
Ser Phe Ile Phe Phe Asn Lys Val Glu Ile Val Gly Met Leu Gln Glu
          85          90          95
Asp Glu Lys Phe Leu Thr Asp Leu Phe Ala Gln Leu Thr Asp Glu Ala
          100          105          110
Thr Asp Glu Glu Lys Arg Gln Glu Leu Val Asn Phe Leu Lys Glu Phe
          115          120          125
Cys Ala Phe Ser Gln Thr Leu Gln Pro Gln Asn Arg Asp Ala Phe Phe
          130          135          140
Lys Thr Leu Ser Asn Met Gly Ile Leu Pro Ala Leu Glu Val Ile Leu
          145          150          155          160
Gly Met Asp Asp Thr Gln Val Arg Ser Ala Ala Thr Asp Ile Phe Ser
          165          170          175
Tyr Leu Val Glu Tyr Asn Pro Ser Met Val Arg Glu Phe Val Met Gln
          180          185          190
Glu Ala Gln Gln Asn Asp Asp Val Ser Lys Lys Leu Thr Glu Gln Lys
          195          200          205
Ile Thr Ser Lys Val Asn Ile Ile Cys Thr Asn Ser Lys Tyr Leu Tyr
          210          215          220
Ile Gly Ser Tyr Asn Cys Phe Tyr Tyr Ser Leu Leu Arg Phe Asn Cys
          225          230          235          240
Cys Cys Leu Gly Lys Val
          245 246

```

<210> 133  
 <211> 111  
 <212> PRT  
 <213> Homo sapiens

```

<400> 133
Met Val Tyr Ile Leu Thr Ile Thr Thr Pro Leu Lys Asn Ser Asp Ser
 1          5          10          15

```

```

Arg Lys Arg Lys Ala Val Ile Leu Thr Ala Arg Val His Pro Gly Glu
      20      25      30
Thr Asn Ser Ser Trp Ile Met Lys Gly Leu Leu Asp Tyr Ile Leu Gly
      35      40      45
Asn Ser Ser Asp Ala Gln Leu Leu Arg Asp Thr Phe Val Phe Lys Val
      50      55      60
Val Pro Met Leu Asn Pro Asp Gly Val Ile Val Gly Asn Tyr Arg Cys
      65      70      75      80
Ser Leu Ala Gly Arg Asp Leu Asn Arg Asn Tyr Thr Ser Leu Leu Lys
      85      90      95
Glu Ser Phe Pro Ser Val Trp Tyr Thr Arg Asn Met Val His Arg
      100      105      110 111

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<210> 134
<211> 180
<212> PRT
<213> Homo sapiens

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```

<400> 134
Met Lys Met Gln Val Ser Phe Thr Arg Glu Gly Ser Leu Leu Leu Arg
 1      5      10      15
Leu Ile Thr Val Leu Cys Cys Phe Lys Ile Ser Pro Ile Met Ser Ala
      20      25      30
Leu Ala Leu Glu Ala Ala Ser Phe Leu Arg Ser Gly Leu Ser His Ser
      35      40      45
Thr Thr His Ile Thr Leu Ile Ser Ser Ile Ile Thr Ala Ser Ile Ser
      50      55      60
Ser Lys Gly Gly Leu Leu Pro Val Pro Ile Pro His Pro Ser His Ile
      65      70      75      80
Glu Met Leu Leu Leu Thr Ser Cys Leu Ile Trp Arg Ile Asn Leu Asn
      85      90      95
Lys Pro Pro Ser Pro Trp Ser Ser Tyr Gln Ser Pro Ser Pro Thr Pro
      100      105      110
Ser Ser Ser Trp Ser Pro Gly Gly Gly Tyr Gly Gly Trp Gly Gly
      115      120      125
Ser Gln Gly Arg Asp His Arg Arg Gly Leu Asn Gly Gly Ile Thr Pro
      130      135      140
Leu Asn Ser Ile Ser Pro Leu Lys Lys Asn Phe Ala Ser Asn His Ile
      145      150      155      160
Gln Leu Gln Lys Tyr Ala Arg Pro Ser Ser Ala Phe Ala Pro Lys Ser
      165      170      175
Trp Asp Gly Arg
      180

```

```

<210> 135
<211> 38
<212> PRT
<213> Homo sapiens

```

```

<400> 135
Met Thr Pro Phe Phe His Ile Leu Gly Tyr Lys Ala Leu Ser Pro His
 1      5      10      15
Ile Val Ser Arg Leu Arg Trp Arg Ile Asn Ala Leu Ser Val Gly His
      20      25      30
Ala Tyr Arg Ile Val Asp
      35      38

```

```

<210> 136

```

<211> 112  
 <212> PRT  
 <213> Homo sapiens

<400> 136  
 Met Leu Cys Ala Asn Ile Ser Leu Ala Cys Ile Ile Lys Ser Lys Cys  
 1 5 10 15  
 Lys Thr Leu Val Cys Val Thr Tyr Ala Leu Phe Gly Phe Ile Leu Gln  
 20 25 30  
 Val Gln Tyr Leu Gln Lys Ser Lys Tyr Pro Phe Phe Ile Pro Ala Ser  
 35 40 45  
 Ser Glu Phe Ile Tyr Val Ile Glu Gln Ile Val Ile Glu Asp Ser Leu  
 50 55 60  
 Leu Lys Gln Val Val Gln Ala Met Leu Tyr Ser Phe Leu Tyr Leu Leu  
 65 70 75 80  
 Gly Lys Cys Glu Leu Ile Leu Asp Thr Phe Tyr Pro Asp Pro Gln Trp  
 85 90 95  
 Ser Phe Ser Asn Tyr Ile Leu Leu Ile Ser Ser Phe Cys Phe Leu Val  
 100 105 110 112

<210> 137  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<400> 137  
 Met Ala Ala Phe Ser Gly Leu Ala Glu Ile Ser Leu Leu Asn Pro Gln  
 1 5 10 15  
 Glu Asp Val Gln Phe Gln Lys Glu Val Ala Gln Val Cys Lys His Ile  
 20 25 30  
 Thr Gln Gln Lys Lys Gln Glu Gln Pro Tyr Leu Thr Lys Pro Arg Ser  
 35 40 45  
 Phe His Ile Ser Pro Ser Leu Ala Leu  
 50 55 57

<210> 138  
 <211> 273  
 <212> PRT  
 <213> Homo sapiens

<400> 138  
 Met Gly Thr Gly Ala Leu Arg Ser Ala Gln Ile Trp Ser Leu Ala Ser  
 1 5 10 15  
 Pro Leu Arg Ser Ser Ser Ala Leu Gly Asp His Leu Glu Pro Pro Tyr  
 20 25 30  
 Glu Ile Glu Ala Arg Asp Phe Leu Ala Gly Gln Ser Asp Thr Pro Ala  
 35 40 45  
 Ala Gln Met Pro Ala Leu Phe Pro Arg Glu Gly Cys Pro Gly Asp Gln  
 50 55 60  
 Val Thr Pro Thr Arg Ser Leu Thr Ala Gln Leu Gln Glu Thr Met Thr  
 65 70 75 80  
 Phe Lys Asp Val Glu Val Thr Phe Ser Gln Asp Glu Trp Gly Trp Leu  
 85 90 95  
 Asp Ser Ala Gln Arg Asn Leu Tyr Arg Asp Val Met Leu Glu Asn Tyr  
 100 105 110  
 Arg Asn Met Ala Ser Leu Val Gly Pro Phe Thr Lys Pro Ala Leu Ile

```

      115      120      125
Ser Trp Leu Gly Ala Arg Glu Pro Trp Gly Leu Asn Met Gln Ala Ala
  130      135      140
Gln Pro Lys Gly Asn Pro Val Ala Ala Pro Thr Gly Asp Asp Leu Gln
145      150      155      160
Gly Lys Thr Asn Lys Phe Ile Leu Asn Gln Glu Pro Leu Glu Glu Ala
      165      170      175
Glu Thr Leu Ala Val Ser Ser Gly Cys Pro Ala Thr Ser Val Ser Glu
      180      185      190
Gly Ile Gly Leu Arg Glu Ser Phe Gln Gln Lys Ser Arg Gln Lys Asp
      195      200      205
Gln Cys Glu Asn Pro Ile Gln Val Arg Val Lys Lys Glu Glu Thr Asn
      210      215      220
Phe Ser His Arg Thr Gly Lys Asp Ser Glu Val Ser Gly Ser Asn Ser
225      230      235      240
Leu Asp Leu Lys His Val Thr Tyr Leu Arg Val Ser Gly Arg Lys Glu
      245      250      255
Ser Leu Lys His Gly Cys Gly Lys His Phe Arg Asn Lys Phe Thr Thr
      260      265      270
Val
273

```

```

<210> 139
<211> 211
<212> PRT
<213> Homo sapiens

```

```

<400> 139
Met Gly Ile Trp Asn Ser His Thr Ser Val Gly Asp Ile Leu Gly Ser
  1      5      10      15
Leu Ile Ala Gly Ile Trp Val Asn Gly Gln Trp Gly Leu Ser Phe Ile
      20      25      30
Val Pro Gly Ile Ile Thr Ala Val Met Gly Val Ile Thr Phe Leu Phe
      35      40      45
Leu Ile Glu His Pro Glu Asp Val Asp Cys Ala Pro Pro Gln His His
      50      55      60
Gly Glu Pro Ala Glu Asn Gln Asp Asn Pro Glu Asp Pro Gly Asn Ser
      65      70      75      80
Pro Cys Ser Ile Thr Glu Ser Gly Leu Glu Thr Val Ala Lys Cys Ser
      85      90      95
Lys Gly Pro Cys Glu Glu Pro Ala Ala Ile Ser Phe Phe Gly Ala Leu
      100      105      110
Arg Ile Pro Gly Val Asp Glu Phe Ser Leu Cys Leu Leu Ile Ala Lys
      115      120      125
Leu Val Ser Tyr Thr Phe Leu Tyr Trp Leu Pro Leu Tyr Ile Ala Asn
      130      135      140
Val Ala His Phe Ser Ala Lys Glu Ala Gly Asp Leu Ser Thr Leu Phe
145      150      155      160
His Val Gly Gly Ile Ile Gly Gly Ile Glu Ala Gly Leu Val Ser Asp
      165      170      175
Tyr Thr Asn Gly Arg Ala Thr Thr Cys Cys Val Met Leu Ile Leu Ala
      180      185      190
Ala Pro Met Met Phe Leu Tyr Asn Tyr Ile Gly Gln Asp Gly Ile Ala
      195      200      205
Ser Ser Ile
210 211

```

```

<210> 140
<211> 603
<212> PRT

```

&lt;213&gt; Homo sapiens

&lt;400&gt; 140

```

Met His Gln His Glu Gly His Ile Pro Asn Ala Val Asp Ser Cys Leu
 1      5      10      15
Gln Lys Ile Phe Leu Thr Val Thr Ala Asp Leu Asn Cys Asn Leu Phe
 20      25      30
Ser Lys Glu Gln Arg Ala Tyr Ile Thr Thr Leu Cys Pro Ser Ile Arg
 35      40      45
Lys Met Glu Gly His Asp Gly Ile Glu Lys Val Cys Gly Asp Phe Gln
 50      55      60
Asp Ile Glu Arg Ile His Gln Phe Leu Ser Glu Gln Phe Leu Glu Ser
 65      70      75      80
Glu Gln Lys Gln Gln Phe Ser Pro Ser Met Thr Glu Arg Lys Pro Leu
 85      90      95
Ser Gln Gln Glu Arg Asp Ser Cys Ile Ser Pro Ser Glu Pro Glu Thr
 100     105     110
Lys Ala Glu Gln Lys Ser Asn Tyr Phe Glu Val Pro Leu Pro Tyr Phe
 115     120     125
Glu Tyr Phe Lys Tyr Ile Cys Pro Asp Lys Ile Asn Ser Ile Glu Lys
 130     135     140
Arg Phe Gly Val Asn Ile Glu Ile Gln Glu Ser Ser Pro Asn Met Val
 145     150     155     160
Cys Leu Asp Phe Thr Ser Ser Arg Ser Gly Asp Leu Glu Ala Ala Arg
 165     170     175
Glu Ser Phe Ala Ser Glu Phe Gln Lys Asn Thr Glu Pro Leu Lys Gln
 180     185     190
Glu Cys Val Ser Leu Ala Asp Ser Lys Gln Ala Asn Lys Phe Lys Gln
 195     200     205
Glu Leu Asn His Gln Phe Thr Lys Leu Leu Ile Lys Glu Lys Gly Gly
 210     215     220
Glu Leu Thr Leu Leu Gly Thr Gln Asp Asp Ile Ser Ala Ala Lys Gln
 225     230     235     240
Lys Ile Ser Glu Ala Phe Val Lys Ile Pro Val Lys Leu Phe Ala Ala
 245     250     255
Asn Tyr Met Met Asn Val Ile Glu Val Asp Ser Ala His Tyr Lys Leu
 260     265     270
Leu Glu Thr Glu Leu Leu Gln Glu Ile Ser Glu Ile Glu Lys Arg Tyr
 275     280     285
Asp Ile Cys Ser Lys Val Ser Glu Lys Gly Gln Lys Thr Cys Ile Leu
 290     295     300
Phe Glu Ser Lys Asp Arg Gln Val Asp Leu Ser Val His Ala Tyr Ala
 305     310     315     320
Ser Phe Ile Asp Ala Phe Gln His Ala Ser Cys Gln Leu Met Arg Glu
 325     330     335
Val Leu Leu Leu Lys Ser Leu Gly Lys Glu Arg Lys His Leu His Gln
 340     345     350
Thr Lys Phe Ala Asp Asp Phe Arg Lys Arg His Pro Asn Val His Phe
 355     360     365
Val Leu Asn Gln Glu Ser Met Thr Leu Thr Gly Leu Pro Asn His Leu
 370     375     380
Ala Lys Ala Lys Gln Tyr Val Leu Lys Gly Gly Gly Met Ser Ser Leu
 385     390     395     400
Ala Gly Lys Lys Leu Lys Glu Gly His Glu Thr Pro Met Asp Ile Asp
 405     410     415
Ser Asp Asp Ser Lys Ala Ala Ser Pro Pro Leu Lys Gly Ser Val Ser
 420     425     430
Ser Glu Ala Ser Glu Leu Asp Lys Lys Glu Lys Gly Ile Cys Val Ile
 435     440     445
Cys Met Asp Thr Ile Ser Asn Lys Lys Val Leu Pro Lys Cys Lys His
 450     455     460
Glu Phe Cys Ala Pro Cys Ile Asn Lys Ala Met Ser Tyr Lys Pro Ile

```

465					470					475					480
Cys	Pro	Thr	Cys	Gln	Thr	Ser	Tyr	Gly	Ile	Gln	Lys	Gly	Asn	Gln	Pro
				485					490					495	
Glu	Gly	Ser	Met	Val	Phe	Thr	Val	Ser	Arg	Asp	Ser	Leu	Pro	Gly	Tyr
			500					505					510		
Glu	Ser	Phe	Gly	Thr	Ile	Val	Ile	Thr	Tyr	Ser	Met	Lys	Ala	Gly	Ile
		515						520				525			
Gln	Thr	Glu	Glu	His	Pro	Asn	Pro	Gly	Lys	Arg	Tyr	Pro	Gly	Ile	Gln
		530				535					540				
Arg	Thr	Ala	Tyr	Leu	Pro	Asp	Asn	Lys	Glu	Gly	Arg	Lys	Val	Leu	Lys
545					550					555					560
Leu	Leu	Tyr	Arg	Ala	Phe	Asp	Gln	Lys	Leu	Ile	Phe	Thr	Gly	Gly	Tyr
			565						570					575	
Ser	Arg	Val	Leu	Gly	Val	Ser	Asp	Val	Ile	Thr	Trp	Asn	Asp	Ile	His
		580						585					590		
His	Lys	Thr	Ser	Arg	Phe	Gly	Gly	Pro	Glu	Met					
		595					600			603					

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<210> 141
<211> 301
<212> PRT
<213> Homo sapiens
```

<400> 141																
Met	Asn	Gly	Glu	Gln	Gln	Leu	Asp	Ala	Asp	Ala	Gly	Ser	Gly	Met	Glu	
1				5					10					15		
Glu	Val	Glu	Leu	Ser	Trp	Glu	Asp	Tyr	Leu	Glu	Glu	Thr	Gly	Ser	Thr	
			20					25					30			
Ala	Val	Pro	Tyr	Gly	Ser	Phe	Lys	His	Val	Asp	Thr	Arg	Leu	Gln	Asn	
		35					40					45				
Gly	Phe	Ala	Pro	Gly	Met	Lys	Leu	Glu	Val	Ala	Val	Arg	Thr	Asp	Pro	
	50					55					60					
Glu	Thr	Tyr	Trp	Val	Ala	Thr	Val	Ile	Thr	Thr	Cys	Glu	Gln	Leu	Leu	
65					70					75					80	
Leu	Leu	Arg	Tyr	Asp	Gly	Tyr	Gly	Glu	Asp	Arg	Arg	Ala	Asp	Phe	Trp	
				85					90					95		
Cys	Asp	Ile	Arg	Lys	Ala	Asp	Leu	Tyr	Pro	Ile	Gly	Trp	Cys	Glu	Gln	
			100					105					110			
Asn	Lys	Lys	Thr	Leu	Glu	Ala	Pro	Glu	Gly	Ile	Arg	Asp	Lys	Val	Ser	
	115						120					125				
Asp	Trp	Asp	Glu	Phe	Leu	Arg	Gln	Thr	Leu	Ile	Gly	Ala	Cys	Ser	Pro	
	130					135					140					
Pro	Val	Pro	Leu	Leu	Glu	Gly	Leu	Arg	Asn	Gly	Arg	Asn	Pro	Leu	Asp	
145					150					155					160	
Leu	Ile	Ala	Pro	Gly	Ser	Arg	Leu	Glu	Cys	Gln	Ala	Phe	Gln	Asp	Ser	
			165						170					175		
Leu	Ser	Thr	Trp	Ile	Val	Thr	Val	Val	Glu	Asn	Ile	Gly	Gly	Arg	Leu	
			180					185					190			
Lys	Leu	Arg	Tyr	Glu	Gly	Leu	Glu	Ser	Ser	Asp	Asn	Tyr	Glu	His	Trp	
	195						200					205				
Leu	Tyr	Tyr	Leu	Asp	Pro	Phe	Leu	His	His	Val	Gly	Trp	Ala	Ala	Gln	
	210					215					220					
Gln	Gly	Tyr	Glu	Leu	Gln	Pro	Pro	Ser	Ala	Ile	Arg	His	Leu	Lys	Asn	
225					230					235					240	
Glu	Ala	Glu	Trp	Gln	Glu	Ile	Leu	Ala	Lys	Val	Lys	Glu	Glu	Glu	Glu	
			245						250					255		
Glu	Pro	Leu	Pro	Ser	Tyr	Leu	Phe	Lys	Asp	Lys	Gln	Val	Ile	Gly	Ile	
			260					265					270			
His	Thr	Phe	Ser	Val	Asn	Met	Lys	Leu	Glu	Ala	Val	Asp	Pro	Trp	Ser	
	275						280					285				
Pro	Phe	Gly	Ile	Ser	Pro	Ala	Thr	Gly	Cys	Lys	Gly	Phe				



290

295

300 301

<210> 142  
 <211> 333  
 <212> PRT  
 <213> Homo sapiens

<400> 142  
 Met Lys Leu Glu Ala Val Asp Pro Trp Ser Pro Phe Gly Ile Ser Pro  
 1 5 10 15  
 Ala Thr Val Val Lys Val Phe Asp Glu Lys Tyr Phe Leu Val Glu Met  
 20 25 30  
 Asp Asp Leu Arg Pro Glu Asn His Ala Arg Arg Ser Phe Val Cys His  
 35 40 45  
 Ala Asp Ser Pro Gly Ile Phe Pro Val Gln Trp Ser Leu Lys Asn Gly  
 50 55 60  
 Leu His Ile Ser Pro Pro Gly Tyr Pro Ser Gln Asp Phe Asp Trp  
 65 70 75 80  
 Ala Asp Tyr Leu Lys Gln Cys Gly Ala Glu Ala Ala Pro Gln Arg Cys  
 85 90 95  
 Phe Pro Pro Leu Ile Ser Glu His Glu Phe Lys Glu Asn Met Lys Leu  
 100 105 110  
 Glu Ala Val Asn Pro Ile Leu Pro Glu Glu Val Cys Val Ala Thr Ile  
 115 120 125  
 Thr Ala Val Arg Gly Ser Tyr Leu Trp Leu Gln Leu Glu Gly Ser Lys  
 130 135 140  
 Lys Pro Ile Pro Glu Cys Ile Val Ser Val Glu Ser Met Asp Ile Phe  
 145 150 155 160  
 Pro Leu Gly Trp Cys Glu Thr Asn Gly His Pro Leu Ser Thr Pro Arg  
 165 170 175  
 Arg Ala Arg Val Tyr Lys Gln Arg Lys Ile Ala Val Val Gln Pro Glu  
 180 185 190  
 Lys Gln Val Pro Ser Ser Arg Thr Val His Glu Gly Leu Arg Asn Gln  
 195 200 205  
 Glu Leu Asn Ser Thr Glu Ser Val Met Ile Asn Gly Lys Tyr Cys Cys  
 210 215 220  
 Pro Lys Ile Tyr Phe Asn His Arg Cys Phe Ser Gly Pro Tyr Leu Asn  
 225 230 235 240  
 Lys Gly Arg Ile Ala Glu Leu Pro Gln Cys Val Gly Pro Gly Asn Cys  
 245 250 255  
 Val Leu Val Leu Arg Glu Val Leu Thr Leu Leu Ile Asn Ala Ala Tyr  
 260 265 270  
 Lys Pro Ser Arg Val Leu Arg Glu Leu Gln Leu Asp Lys Asp Ser Val  
 275 280 285  
 Trp His Gly Cys Gly Glu Val Leu Lys Ala Lys Tyr Lys Gly Lys Ser  
 290 295 300  
 Tyr Arg Ala Thr Val Glu Ile Val Lys Thr Ala Asp Arg Val Thr Glu  
 305 310 315 320  
 Phe Cys Arg Gln Thr Cys Ile Lys Thr Gly Met Leu Ser  
 325 330 333

<210> 143  
 <211> 92  
 <212> PRT  
 <213> Homo sapiens

<400> 143  
 Met Val Asp Gly Pro His Ser Ser Arg His Val Leu Arg Glu Thr Gly  
 1 5 10 15

Gly Arg Tyr Gln Val Ser Leu Leu Gln Arg Lys Gly Gly Cys Ser Ser  
                   20                  25                  30  
 Pro Gln Leu Cys Cys Asn Gly Asn Ser Val Thr Val Ser His Trp Gly  
           35                  40                  45  
 Leu Val Leu Arg Glu Ala Met Arg Arg Thr Ala Cys Pro Ser Gly Leu  
       50                  55                  60  
 Ser Pro Cys Phe Phe Ile Ser Ser Phe Ser Thr Cys His Leu Arg Arg  
       65                  70                  75                  80  
 Trp Lys Gly Arg Ser Cys Pro Gln Ser Ile Ser Pro  
                   85                  90                  92

<210> 144  
 <211> 1235  
 <212> PRT  
 <213> Homo sapiens

<400> 144  
 Met Lys Glu Leu Met Lys Lys Phe Lys Glu Ile Gln Thr Gln Asn Phe  
   1                  5                  10                  15  
 Ser Leu Ile Asn Glu Asn Gln Ser Leu Lys Lys Asn Ile Ser Ala Leu  
                   20                  25                  30  
 Ile Lys Thr Ala Arg Val Glu Ile Asn Arg Lys Asp Glu Glu Ile Ser  
       35                  40                  45  
 Asn Leu His Gln Arg Leu Ser Glu Phe Pro His Phe Arg Asn Asn His  
       50                  55                  60  
 Lys Thr Ala Arg Thr Phe Asp Thr Val Lys Thr Lys Asp Leu Lys Ser  
       65                  70                  75                  80  
 Arg Ser Pro His Leu Asp Asp Cys Ser Lys Thr Asp His Arg Ala Lys  
                   85                  90                  95  
 Ser Asp Val Ser Lys Asp Val His His Ser Thr Ser Leu Pro Asn Leu  
                   100                  105                  110  
 Glu Lys Glu Gly Lys Pro His Ser Asp Lys Arg Ser Thr Ser His Leu  
                   115                  120                  125  
 Pro Thr Ser Val Glu Lys His Cys Thr Asn Gly Val Trp Ser Arg Ser  
       130                  135                  140  
 His Tyr Gln Val Gly Glu Gly Ser Ser Asn Glu Asp Ser Arg Arg Gly  
       145                  150                  155                  160  
 Arg Lys Asp Ile Arg His Ser Gln Phe Asn Arg Gly Thr Glu Arg Val  
                   165                  170                  175  
 Arg Lys Asp Leu Ser Thr Gly Cys Gly Asp Gly Glu Pro Arg Ile Leu  
                   180                  185                  190  
 Glu Ala Ser Gln Arg Leu Gln Gly His Pro Glu Lys Tyr Gly Lys Gly  
                   195                  200                  205  
 Glu Pro Lys Thr Glu Ser Lys Ser Ser Lys Phe Lys Ser Asn Ser Asp  
       210                  215                  220  
 Ser Asp Tyr Lys Gly Glu Arg Ile Asn Ser Ser Trp Glu Lys Glu Thr  
       225                  230                  235                  240  
 Pro Gly Glu Arg Ser His Ser Arg Val Asp Ser Gln Ser Asp Lys Lys  
                   245                  250                  255  
 Leu Glu Arg Gln Ser Glu Arg Ser Gln Asn Ile Asn Arg Lys Glu Val  
                   260                  265                  270  
 Lys Ser Gln Asp Lys Glu Glu Arg Lys Val Asp Gln Lys Pro Lys Ser  
                   275                  280                  285  
 Val Val Lys Asp Gln Asp His Trp Arg Arg Ser Glu Arg Ala Ser Leu  
       290                  295                  300  
 Pro His Ser Lys Asn Glu Ile Thr Phe Ser His Asn Ser Ser Lys Tyr  
       305                  310                  315                  320  
 His Leu Glu Glu Arg Arg Gly Trp Glu Asp Cys Lys Arg Asp Lys Ser  
                   325                  330                  335  
 Val Asn Ser His Ser Phe Gln Asp Gly Arg Cys Pro Ser Ser Leu Ser  
                   340                  345                  350

Asn Ser Arg Thr His Lys Asn Ile Asp Ser Lys Glu Val Asp Ala Met  
 355 360 365  
 His Gln Trp Glu Asn Thr Pro Leu Lys Ala Glu Arg His Arg Thr Glu  
 370 375 380  
 Asp Lys Arg Lys Arg Glu Gln Glu Ser Lys Glu Glu Asn Arg His Ile  
 385 390 395 400  
 Arg Asn Glu Lys Arg Val Pro Thr Glu His Leu Gln Lys Thr Asn Lys  
 405 410 415  
 Glu Thr Lys Lys Thr Thr Thr Asp Leu Lys Lys Gln Asn Glu Pro Lys  
 420 425 430  
 Thr Asp Lys Gly Glu Val Leu Asp Asn Gly Val Ser Glu Gly Ala Asp  
 435 440 445  
 Asn Lys Glu Leu Ala Met Lys Ala Glu Ser Gly Pro Asn Glu Thr Lys  
 450 455 460  
 Asn Lys Asp Leu Lys Leu Ser Phe Met Lys Lys Leu Asn Leu Thr Leu  
 465 470 475 480  
 Ser Pro Ala Lys Lys Gln Pro Val Ser Gln Asp Asn Gln His Lys Ile  
 485 490 495  
 Thr Asp Ile Pro Lys Ser Ser Gly Val Cys Asp Ser Glu Ser Ser Met  
 500 505 510  
 Gln Val Lys Thr Val Ala Tyr Val Pro Ser Ile Ser Glu His Ile Leu  
 515 520 525  
 Gly Glu Ala Ala Val Ser Glu His Thr Met Gly Glu Thr Lys Ser Thr  
 530 535 540  
 Leu Leu Glu Pro Lys Val Ala Leu Leu Ala Val Thr Glu Pro Arg Ile  
 545 550 555 560  
 Gly Ile Ser Glu Thr Asn Lys Glu Asp Glu Asn Ser Leu Leu Val Arg  
 565 570 575  
 Ser Val Asp Asn Thr Met His Cys Glu Glu Pro Ile Cys Gly Thr Glu  
 580 585 590  
 Thr Ser Phe Pro Ser Pro Met Glu Ile Gln Gln Thr Glu Ser Leu Phe  
 595 600 605  
 Pro Ser Thr Gly Met Lys Gln Thr Ile Asn Asn Gly Arg Ala Ala Ala  
 610 615 620  
 Pro Val Val Met Asp Val Leu Gln Thr Asp Val Ser Gln Asn Phe Gly  
 625 630 635 640  
 Leu Glu Leu Asp Thr Lys Arg Asn Asp Asn Ser Asp Tyr Cys Gly Ile  
 645 650 655  
 Ser Glu Gly Met Glu Met Lys Val Ala Leu Ser Thr Thr Val Ser Glu  
 660 665 670  
 Thr Thr Glu Ser Ile Leu Gln Pro Ser Ile Glu Glu Ala Asp Ile Leu  
 675 680 685  
 Pro Ile Met Leu Ser Glu Asp Asn Asn Pro Lys Phe Glu Pro Ser Val  
 690 695 700  
 Ile Val Thr Pro Leu Val Glu Ser Lys Ser Cys His Leu Glu Pro Cys  
 705 710 715 720  
 Leu Pro Lys Glu Thr Leu Asp Ser Ser Leu Gln Gln Thr Glu Leu Met  
 725 730 735  
 Asp His Arg Met Ala Thr Gly Glu Thr Asn Ser Val Tyr His Asp Asp  
 740 745 750  
 Asp Asn Ser Val Leu Ser Ile Asp Leu Asn His Leu Arg Pro Ile Pro  
 755 760 765  
 Glu Ala Ile Ser Pro Leu Asn Ser Pro Val Arg Pro Val Ala Lys Val  
 770 775 780  
 Leu Arg Asn Glu Ser Pro Pro Gln Val Pro Val Tyr Asn Asn Ser His  
 785 790 795 800  
 Lys Asp Val Phe Leu Pro Asn Ser Ala His Ser Thr Ser Lys Ser Gln  
 805 810 815  
 Ser Asp Leu Asn Lys Glu Asn Gln Lys Pro Ile Tyr Lys Ser Asp Lys  
 820 825 830  
 Cys Thr Glu Ala Asp Thr Cys Lys Asn Ser Pro Leu Asp Glu Leu Glu  
 835 840 845  
 Glu Gly Glu Ile Arg Ser Asp Ser Glu Thr Ser Lys Pro Gln Glu Ser

850 855 860  
 Phe Glu Lys Asn Ser Lys Arg Arg Val Ser Ala Asp Val Arg Lys Ser  
 865 870 875 880  
 Lys Thr Ile Pro Arg Arg Gly Lys Ser Thr Val Cys Leu Asp Lys Asp  
 885 890 895  
 Ser Arg Lys Thr His Val Arg Ile His Gln Thr Asn Asn Lys Trp Asn  
 900 905 910  
 Lys Arg Pro Asp Lys Ser Ser Arg Ser Ser Lys Thr Glu Lys Lys Asp  
 915 920 925  
 Lys Val Met Ser Thr Ser Ser Leu Glu Lys Ile Val Pro Ile Ile Ala  
 930 935 940  
 Val Pro Ser Ser Glu Gln Glu Ile Met His Met Leu Arg Met Ile Arg  
 945 950 955 960  
 Lys His Val Arg Lys Asn Tyr Met Lys Phe Lys Ala Lys Phe Ser Leu  
 965 970 975  
 Ile Gln Phe His Arg Ile Ile Glu Ser Ala Ile Leu Ser Phe Thr Ser  
 980 985 990  
 Leu Ile Lys His Leu Asn Leu His Lys Ile Ser Lys Ser Val Thr Thr  
 995 1000 1005  
 Leu Gln Lys Asn Leu Cys Asp Ile Ile Glu Ser Lys Leu Lys Gln Val  
 1010 1015 1020  
 Lys Lys Asn Gly Ile Val Asp Arg Leu Phe Glu Gln Gln Leu Pro Asp  
 1025 1030 1035 1040  
 Met Lys Lys Lys Leu Trp Lys Phe Val Asp Asp Gln Leu Asp Tyr Leu  
 1045 1050 1055  
 Phe Ala Lys Leu Lys Lys Ile Leu Val Cys Asp Ser Lys Ser Phe Gly  
 1060 1065 1070  
 Arg Asp Ser Asp Glu Gly Lys Leu Glu Lys Thr Ser Lys Gln Asn Ala  
 1075 1080 1085  
 Gln Tyr Ser Asn Ser Gln Lys Arg Ser Val Asp Asn Ser Asn Arg Glu  
 1090 1095 1100  
 Leu Leu Lys Glu Lys Leu Ser Lys Ser Glu Asp Pro Val His Tyr Lys  
 1105 1110 1115 1120  
 Ser Leu Val Gly Cys Lys Lys Ser Glu Glu Asn Tyr Gln Asp Gln Asn  
 1125 1130 1135  
 Asn Ser Ser Ile Asn Thr Val Lys His Asp Ile Lys Lys Asn Phe Asn  
 1140 1145 1150  
 Ile Cys Phe Asp Asn Ile Lys Asn Ser Gln Ser Glu Glu Arg Ser Leu  
 1155 1160 1165  
 Glu Val His Cys Pro Ser Thr Pro Lys Ser Glu Lys Asn Glu Gly Ser  
 1170 1175 1180  
 Ser Ile Glu Asp Ala Gln Thr Ser Gln His Ala Thr Leu Lys Pro Glu  
 1185 1190 1195 1200  
 Arg Ser Phe Glu Ile Leu Thr Glu Gln Gln Ala Ser Ser Leu Thr Phe  
 1205 1210 1215  
 Asn Leu Val Ser Asp Ala Gln Met Gly Glu Ile Phe Lys Ser Leu Leu  
 1220 1225 1230  
 Pro Arg Phe  
 1235

<210> 145  
 <211> 161  
 <212> PRT  
 <213> Homo sapiens

<400> 145  
 Met Gln Asp Gly Gly Pro Ser Pro Ala Glu His Ser Lys Ala Glu Glu  
 1 5 10 15  
 Ser Ala Gly Met Glu Ala Arg Phe Leu Gly Leu Pro Asp Ala Ala Gly  
 20 25 30  
 Ser Ser Gly Pro Thr Pro Ala Arg Arg Cys Pro Ala Pro Arg Pro Ala

```

      35      40      45
Gly Val Ser Tyr Val Ile Arg Asp Glu Val Glu Lys Tyr Asn Arg Asn
  50      55      60
Gly Val Asn Ala Leu Gln Leu Asp Pro Ala Leu Asn Arg Leu Phe Thr
  65      70      75      80
Ala Arg Arg Asp Ser Ile Ile Arg Ile Trp Arg Val Asn Gln His Lys
      85      90      95
Gln Asp Pro Tyr Ile Ala Ser Met Glu His His Thr Asp Trp Val Asn
      100      105      110
Asp Ile Val Leu Cys Cys Asn Gly Lys Thr Leu Ile Ser Ala Ser Ser
      115      120      125
Asp Thr Thr Val Lys Val Trp Asn Ala His Lys Gly Phe Cys Met Ser
      130      135      140
Thr Leu Arg Thr His Lys Asp Tyr Val Lys Ala Leu Ala Tyr Ala Lys
      145      150      155      160
Gly
      161

```

<210> 146  
 <211> 91  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 146
Met Pro Phe Ser Ile Ser Phe Ser Ala Ser Leu Leu Val Ile Tyr Phe
  1      5      10      15
Leu Ile Phe Phe Leu Ser Glu Asn Ile Phe Ser Ser Pro Ser Phe Leu
      20      25      30
Lys Gly Ile Pro Phe Tyr Thr Phe Ile Pro Leu Ser Ser Ala Phe His
      35      40      45
Cys Phe Cys Ser Glu Val Ser Cys Gln Pro Cys Cys Cys Ser Thr Glu
      50      55      60
Asp Asn Thr Ser Phe Leu Pro Leu Ala Val Cys Phe Gly Ala His Asn
      65      70      75      80
Ala Ser Val Cys Gly Leu Lys Ser Phe Ile Val
      85      90      91

```

<210> 147  
 <211> 1001  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 147
Met Glu Ser Lys Val Ser Gln Asn Gly Asp Ile Leu Ile Glu Glu Met
  1      5      10      15
Ile Glu Lys Leu Lys Lys Asp Tyr Gln Glu Glu Ile Ala Ile Ala Gln
      20      25      30
Glu Asn Lys Ile Gln Leu Gln Gln Met Gly Glu Arg Leu Ala Lys Ala
      35      40      45
Ser His Glu Ser Lys Ala Ser Glu Ile Glu Tyr Lys Leu Gly Lys Val
      50      55      60
Asn Asp Arg Trp Gln His Leu Leu Asp Leu Ile Ala Ala Arg Val Lys
      65      70      75      80
Lys Leu Lys Glu Thr Leu Val Ala Val Gln Gln Leu Asp Lys Asn Met
      85      90      95
Ser Ser Leu Arg Thr Trp Leu Ala His Ile Glu Ser Glu Leu Ala Lys
      100      105      110
Pro Ile Val Tyr Asp Ser Cys Asn Ser Glu Glu Ile Gln Arg Lys Leu
      115      120      125

```

Asn Glu Gln Gln Glu Leu Gln Arg Asp Ile Glu Lys His Ser Thr Gly  
 130 135 140  
 Val Ala Ser Val Leu Asn Leu Cys Glu Val Leu Leu His Asp Cys Asp  
 145 150 155 160  
 Ala Cys Ala Thr Asp Ala Glu Cys Asp Ser Ile Gln Gln Ala Thr Arg  
 165 170 175  
 Asn Leu Asp Arg Arg Trp Arg Asn Ile Cys Ala Met Ser Met Glu Arg  
 180 185 190  
 Arg Leu Lys Ile Glu Glu Thr Trp Arg Leu Trp Gln Lys Phe Leu Asp  
 195 200 205  
 Asp Tyr Ser Arg Phe Glu Asp Trp Leu Lys Ser Ser Glu Arg Thr Ala  
 210 215 220  
 Ala Phe Pro Ser Ser Ser Gly Val Ile Tyr Thr Val Ala Lys Glu Glu  
 225 230 235 240  
 Leu Lys Lys Phe Glu Ala Phe Gln Arg Gln Val His Glu Cys Leu Thr  
 245 250 255  
 Gln Leu Glu Leu Ile Asn Lys Gln Tyr Arg Arg Leu Ala Arg Glu Asn  
 260 265 270  
 Arg Thr Asp Ser Ala Cys Ser Leu Lys Gln Met Val His Glu Gly Asn  
 275 280 285  
 Gln Arg Trp Asp Asn Leu Gln Lys Arg Val Thr Ser Ile Leu Arg Arg  
 290 295 300  
 Leu Lys His Phe Ile Gly Gln Arg Glu Glu Phe Glu Thr Ala Arg Asp  
 305 310 315 320  
 Ser Ile Leu Val Trp Leu Thr Glu Met Asp Leu Gln Leu Thr Asn Ile  
 325 330 335  
 Glu His Phe Ser Glu Cys Asp Val Gln Ala Lys Ile Lys Gln Leu Lys  
 340 345 350  
 Ala Phe Gln Gln Glu Ile Ser Leu Asn His Asn Lys Ile Glu Gln Ile  
 355 360 365  
 Ile Ala Gln Gly Glu Gln Leu Ile Glu Lys Ser Glu Pro Leu Asp Ala  
 370 375 380  
 Ala Ile Ile Glu Glu Glu Leu Asp Glu Leu Arg Arg Tyr Cys Gln Glu  
 385 390 395 400  
 Val Phe Gly Arg Val Glu Arg Tyr His Lys Lys Leu Ile Arg Leu Pro  
 405 410 415  
 Leu Pro Asp Asp Glu His Asp Leu Ser Asp Arg Glu Leu Glu Leu Glu  
 420 425 430  
 Asp Ser Ala Ala Leu Ser Asp Leu His Trp His Asp Arg Ser Ala Asp  
 435 440 445  
 Ser Leu Leu Ser Pro Gln Pro Ser Ser Asn Leu Ser Leu Ser Leu Ala  
 450 455 460  
 Gln Pro Leu Arg Ser Glu Arg Ser Gly Arg Asp Thr Pro Ala Ser Val  
 465 470 475 480  
 Asp Ser Ile Pro Leu Glu Trp Asp His Asp Tyr Asp Leu Ser Arg Asp  
 485 490 495  
 Leu Glu Ser Ala Met Ser Arg Ala Leu Pro Ser Glu Asp Glu Glu Gly  
 500 505 510  
 Gln Asp Asp Lys Asp Phe Tyr Leu Arg Gly Ala Val Ala Leu Ser Gly  
 515 520 525  
 Asp His Ser Ala Leu Glu Ser Gln Ile Arg Gln Leu Gly Lys Ala Leu  
 530 535 540  
 Asp Asp Ser Arg Phe Gln Ile Gln Gln Thr Glu Asn Ile Ile Arg Ser  
 545 550 555 560  
 Lys Thr Pro Thr Gly Pro Glu Leu Asp Thr Ser Tyr Lys Gly Tyr Met  
 565 570 575  
 Lys Leu Leu Gly Glu Cys Ser Ser Ser Ile Asp Ser Val Lys Arg Leu  
 580 585 590  
 Glu His Lys Leu Lys Glu Glu Glu Ser Leu Pro Gly Phe Val Asn  
 595 600 605  
 Leu His Ser Thr Glu Thr Gln Thr Ala Gly Val Ile Asp Arg Trp Glu  
 610 615 620  
 Leu Leu Gln Ala Gln Ala Leu Ser Lys Glu Leu Arg Met Lys Gln Asn

```

625          630          635          640
Leu Gln Lys Trp Gln Gln Phe Asn Ser Asp Leu Asn Ser Ile Trp Ala
          645          650          655
Trp Leu Gly Asp Thr Glu Glu Glu Leu Glu Gln Leu Gln Arg Leu Glu
          660          665          670
Leu Ser Thr Asp Ile Gln Thr Ile Glu Leu Gln Ile Lys Lys Leu Lys
          675          680          685
Glu Leu Gln Lys Ala Val Asp His Arg Lys Ala Ile Ile Leu Ser Ile
          690          695          700
Asn Leu Cys Ser Pro Glu Phe Thr Gln Ala Asp Ser Lys Glu Ser Arg
705          710          715          720
Asp Leu Gln Asp Arg Leu Ser Gln Met Asn Gly Arg Trp Asp Arg Val
          725          730          735
Cys Ser Leu Leu Glu Glu Trp Arg Gly Leu Leu Gln Asp Ala Leu Met
          740          745          750
Gln Cys Gln Gly Phe His Glu Met Ser His Gly Leu Leu Met Leu
          755          760          765
Glu Asn Ile Asp Arg Arg Lys Asn Glu Ile Val Pro Ile Asp Ser Asn
          770          775          780
Leu Asp Ala Glu Ile Leu Gln Asp His His Lys Gln Leu Met Gln Ile
785          790          795          800
Lys His Glu Leu Leu Glu Ser Gln Leu Arg Val Ala Ser Leu Gln Asp
          805          810          815
Met Ser Cys Gln Leu Leu Val Asn Ala Glu Gly Thr Asp Cys Leu Glu
          820          825          830
Ala Lys Glu Lys Val His Val Ile Gly Asn Arg Leu Lys Leu Leu Leu
          835          840          845
Lys Glu Val Ser Arg His Ile Lys Glu Leu Glu Lys Leu Leu Asp Val
          850          855          860
Ser Ser Ser Gln Gln Asp Leu Ser Ser Trp Ser Ser Ala Asp Glu Leu
865          870          875          880
Asp Thr Ser Gly Ser Val Ser Pro Thr Ser Gly Arg Ser Thr Pro Asn
          885          890          895
Arg Gln Lys Thr Pro Arg Gly Lys Cys Ser Leu Ser Gln Pro Gly Pro
          900          905          910
Ser Val Ser Ser Pro His Ser Arg Ser Thr Lys Gly Gly Ser Asp Ser
          915          920          925
Ser Leu Ser Glu Pro Gly Pro Gly Arg Ser Gly Arg Gly Phe Leu Phe
          930          935          940
Arg Val Leu Arg Ala Ala Leu Pro Leu Gln Leu Leu Leu Leu Leu Leu
945          950          955          960
Ile Gly Leu Ala Met Pro Cys Thr Asn Val Arg Gly Arg Leu Gln Leu
          965          970          975
Cys Pro Leu Gln Gln Leu Cys Pro Val Ile Pro Pro His Ala Gln Met
          980          985          990
His Glu Trp Pro Ser Ser Thr Leu Asn
          995          10001001

```

<210> 148  
 <211> 135  
 <212> PRT  
 <213> Homo sapiens

```

<400> 148
Met Lys Ser Leu Ser Ser Arg Pro Pro Ser Pro Ser Leu Thr Glu Met
1          5          10          15
Gly Ile Val Phe Trp Met Arg Arg Asn Arg Lys Lys Cys Asp Arg Thr
          20          25          30
Trp Arg Lys Arg Gly Leu Thr Arg Arg Val Leu Gln Leu Glu Thr Val
          35          40          45
Leu Glu Arg Val Val Ala Gln Ile Asp Ala Val Gly Ser Lys Leu Lys

```

```

      50              55              60
Met Leu Glu Arg Lys Gly Trp Leu Ala Pro Ser Pro Gly Val Lys Glu
 65              70              75              80
Gln Ala Ile Trp Lys His Pro Gln Pro Ala Pro Ala Val Thr Pro Asp
      85              90              95
Pro Trp Gly Val Gln Gly Gly Gln Glu Ser Gly Glu Glu Gly Gly Leu
      100              105              110
Lys His Gln Thr Ala Gly Phe Pro Pro Ser Ala Ser Ala Gln Ala Pro
      115              120              125
Ser Pro His Pro Leu His Phe
      130              135

```

<210> 149  
 <211> 642  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 149
Met Lys Lys Phe Gly Gly Pro Gly Arg Met Lys Gln Ser Cys Ile Met
 1              5              10              15
Arg Gln Cys Ile Ala Pro Val Leu Pro His Thr Ala Val Cys Leu Val
      20              25              30
Cys Gly Glu Ala Gly Lys Glu Asp Thr Val Glu Glu Glu Gly Lys
      35              40              45
Phe Asn Leu Met Leu Met Glu Cys Ser Ile Cys Asn Glu Ile Ile His
      50              55              60
Pro Gly Cys Leu Lys Ile Lys Glu Ser Glu Gly Val Val Asn Asp Glu
      65              70              75              80
Leu Pro Asn Cys Trp Glu Cys Pro Lys Cys Asn His Ala Gly Lys Thr
      85              90              95
Gly Lys Ala Tyr Lys Gln Lys Arg Gly Pro Gly Phe Lys Tyr Ala Ser
      100              105              110
Asn Leu Pro Gly Ser Leu Leu Lys Glu Gln Lys Met Asn Arg Asp Asn
      115              120              125
Lys Glu Gly Gln Glu Pro Ala Lys Arg Arg Ser Glu Cys Glu Glu Ala
      130              135              140
Pro Arg Arg Arg Ser Asp Glu His Ser Lys Lys Val Pro Pro Asp Gly
      145              150              155              160
Leu Leu Arg Arg Lys Ser Asp Asp Val His Leu Arg Lys Lys Arg Lys
      165              170              175
Tyr Glu Lys Pro Gln Glu Leu Ser Gly Arg Lys Arg Ala Ser Ser Leu
      180              185              190
Gln Thr Ser Pro Gly Ser Ser Ser His Leu Ser Pro Arg Pro Pro Leu
      195              200              205
Gly Ser Ser Leu Ser Pro Trp Trp Arg Ser Ser Leu Thr Tyr Phe Gln
      210              215              220
Gln Gln Leu Lys Pro Gly Lys Glu Asp Lys Leu Phe Arg Lys Lys Arg
      225              230              235              240
Arg Ser Trp Lys Asn Ala Glu Asp Arg Met Ala Leu Ala Asn Lys Pro
      245              250              255
Leu Arg Arg Phe Lys Gln Glu Pro Glu Asp Glu Leu Pro Glu Ala Pro
      260              265              270
Pro Lys Thr Arg Glu Ser Asp His Ser Arg Ser Ser Ser Pro Thr Ala
      275              280              285
Gly Pro Ser Thr Glu Gly Ala Glu Gly Pro Glu Glu Lys Lys Lys Val
      290              295              300
Lys Met Arg Arg Lys Arg Arg Leu Pro Asn Lys Glu Leu Ser Arg Glu
      305              310              315              320
Leu Ser Lys Glu Leu Asn His Glu Ile Gln Arg Thr Glu Asn Ser Leu
      325              330              335
Ala Asn Glu Asn Gln Gln Pro Ile Lys Ser Glu Pro Glu Ser Glu Gly

```



```

      340      345      350
Glu Glu Pro Lys Arg Pro Pro Gly Ile Cys Glu Arg Pro His Arg Phe
      355      360      365
Ser Lys Gly Leu Asn Gly Thr Pro Arg Glu Leu Arg His Gln Leu Gly
      370      375      380
Pro Ser Leu Arg Ser Pro Pro Arg Val Ile Ser Arg Pro Pro Pro Ser
385      390      395      400
Val Ser Pro Pro Lys Cys Ile Gln Met Glu Arg His Val Ile Arg Pro
      405      410      415
Pro Pro Ile Ser Pro Pro Pro Asp Ser Leu Pro Leu Asp Asp Gly Ala
      420      425      430
Ala His Val Met His Arg Glu Val Trp Met Ala Val Phe Ser Tyr Leu
      435      440      445
Ser His Gln Asp Leu Cys Val Cys Met Arg Val Cys Arg Thr Trp Asn
450      455      460
Arg Trp Cys Cys Asp Lys Arg Leu Trp Thr Arg Ile Asp Leu Asn His
465      470      475      480
Cys Lys Ser Ile Thr Pro Leu Met Leu Ser Gly Ile Ile Arg Arg Gln
      485      490      495
Pro Val Ser Leu Asp Leu Ser Trp Thr Asn Ile Ser Lys Lys Gln Leu
      500      505      510
Ser Trp Leu Ile Asn Arg Leu Ala Trp Ala Pro Gly Leu Gly Ala Val
      515      520      525
Arg Leu Leu Met Asp Arg Gly Leu Gly Pro Phe Ala Ala Pro Val Val
530      535      540
Arg Cys Ser Gly Asn Leu Asp Val Gln Val Gly Gly Gly Thr Lys Gly
545      550      555      560
Met Pro Arg Cys Gly Ile Ser Cys Pro Arg Pro Gln Thr Thr Gly Gln
      565      570      575
Val Arg Trp Thr Ile Gly Ala Ser Ser Gly Thr Ser Trp Ser Cys Ala
      580      585      590
Trp Gln Ala Trp Thr Ser Gln Met Pro Pro Cys Gly Ser Ser Ser Ala
      595      600      605
Thr Cys Pro Cys Ser Pro Ser Ser Thr Ser Val Thr Val Thr Thr Ser
610      615      620
Pro Thr Ser Leu Ser Thr Cys Ser Leu Leu Leu Ala Pro Pro Pro Glu
625      630      635      640
Thr Pro
642

```

<210> 150  
 <211> 65  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 150
Met Trp Ile Arg Pro Lys Ser Ile Asn Arg Leu Pro Phe Gly Ala Gln
  1      5      10      15
Gly Trp Met Leu Ser Leu Ile Thr Thr Lys Pro Arg Thr Gly Leu Asn
      20      25      30
Lys Glu Gln Ala Val Pro Leu Ser Phe Ser Trp Lys Arg Arg Gly Arg
      35      40      45
Arg Leu Leu Val Arg Asp Tyr Trp Glu Gly Pro Glu Leu Gln Arg Pro
50      55      60
Gln
65

```

<210> 151  
 <211> 129  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 151

```

Met Gly Leu Gly Leu Ser Cys Val Ser Ile Leu Ile Arg Lys Gly Tyr
 1          5          10          15
Ala His Thr Leu Ala Cys Ser Asp Ser Lys Thr Glu Gly Phe Thr Arg
          20          25          30
Pro Thr Pro Gly Lys Trp Ala Ser Leu Pro Pro Met Leu Ser Phe Asn
          35          40          45
Leu Cys Asn Leu Pro Val Ser Ile Gly Gly His Leu Thr Pro Ser Lys
          50          55          60
Glu Pro Ser Leu Ser Leu Ser Leu Tyr Pro Cys Asn Ser Leu Leu Cys
          65          70          75          80
Ala Phe Pro Gln Ala Gly Pro Ser Ser Thr Leu His Leu Gly Leu Leu
          85          90          95
Ile Thr Pro Leu Pro Thr His His Cys Cys Ser Ser Arg Ala Ser Thr
          100          105          110
Arg Ala Arg Gln Gly Ser Cys Leu Arg Tyr Ile Asn Leu Lys Gly His
          115          120          125
Ser
129

```

&lt;210&gt; 152

&lt;211&gt; 245

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 152

```

Met Cys Ile Gln Ala Asp Cys Ser Arg Pro Gln Ser Cys Arg Ala Phe
 1          5          10          15
Arg Thr His Ser Ser Asn Ser Met Leu Val Phe Leu Lys Lys Phe Gln
          20          25          30
Thr Ala Asp Asp Leu Gly Phe Leu Pro Glu Asp Asp Val Pro His Leu
          35          40          45
Leu Gly Leu Gly Trp Asn Trp Ala Ser Trp Arg Gln Ser Pro Pro Arg
          50          55          60
Ala Ala Leu Arg Pro Ala Val Ser Ser Ser Asp Gln Gln Ser Leu Ile
          65          70          75          80
Arg Lys Leu Gln Lys Arg Gly Ser Pro Ser Asp Val Val Thr Pro Ile
          85          90          95
Val Thr Gln His Ser Lys Val Asn Asp Ser Asn Glu Leu Gly Gly Leu
          100          105          110
Thr Thr Ser Gly Ser Ala Glu Val His Lys Ala Ile Thr Ile Ser Ser
          115          120          125
Pro Leu Thr Thr Asp Leu Thr Ala Glu Leu Ser Gly Gly Pro Lys Asn
          130          135          140
Val Ser Val Gln Pro Glu Ile Ser Glu Gly Leu Ala Thr Thr Pro Ser
          145          150          155          160
Thr Gln Gln Val Lys Ser Ser Glu Lys Thr Gln Ile Ala Val Pro Gln
          165          170          175
Pro Val Ala Pro Ser Tyr Ser Tyr Ala Thr Pro Thr Pro Gln Ala Ser
          180          185          190
Phe Gln Ser Thr Ser Ala Pro Tyr Pro Val Ile Lys Glu Leu Val Val
          195          200          205
Ser Ala Gly Glu Ser Val Gln Ile Thr Leu Pro Lys Asn Glu Val Gln
          210          215          220
Leu Asn Ala Tyr Gly Ser Ser Arg Asn His Leu Lys Glu Lys Pro Thr
          225          230          235          240
Pro Thr Thr Gly Ser
          245

```

<210> 153  
 <211> 142  
 <212> PRT  
 <213> Homo sapiens

<400> 153  
 Met Pro Val Cys Cys Leu Thr Ser Glu Lys Asp Gly Ser Leu Asn Val  
 1 5 10 15  
 Phe Ser Asn Asp Ile Val Gly Leu Pro Thr Ser Thr Cys Leu His Lys  
 20 25 30  
 Thr Val Cys His Leu Asp Pro Trp Val Cys Ala Pro Pro Ser Asp Lys  
 35 40 45  
 Ile Leu Leu Trp Ile Trp Asp Leu Leu Leu Leu Glu Thr Ala Pro Gly  
 50 55 60  
 Pro Trp Pro Cys Thr Ala Ala Pro Val Cys Arg Pro Gly Ser Ser  
 65 70 75 80  
 Arg Met Arg Gln Pro Pro Arg Gln Ser Gln Thr Ser Ala Arg Cys Ala  
 85 90 95  
 Ser Ser Gly Glu Pro Cys His Arg Thr Arg Gln Lys Ala Leu Ala Cys  
 100 105 110  
 Trp His Trp Glu Glu Arg Asp Gln Lys Ser Gln Pro Leu Val Leu Tyr  
 115 120 125  
 Cys Pro Lys Ile Tyr Thr Glu Ile Ala Arg Gln Ser Phe Gln  
 130 135 140 142

<210> 154  
 <211> 55  
 <212> PRT  
 <213> Homo sapiens

<400> 154  
 Met Leu Tyr Phe Cys Tyr Leu Phe Phe Thr Ser Val Val Val Arg Glu  
 1 5 10 15  
 His Ile Leu His Val Ser Arg Pro Gly Leu Trp Ser Val Leu Val Ser  
 20 25 30  
 Val Pro Gly Ala Leu Gly Lys Asp Val Pro Ser Thr Val Leu Gly Tyr  
 35 40 45  
 Arg Ile Tyr Met Ser Leu Gly  
 50 55

<210> 155  
 <211> 444  
 <212> PRT  
 <213> Homo sapiens

<400> 155  
 Met Gly Gln Pro Gly Pro Ser Gly Asp Ser Asp Leu Ala Thr Ala Leu  
 1 5 10 15  
 His Arg Leu Ser Leu Arg Arg Gln Asn Tyr Leu Ser Glu Lys Gln Phe  
 20 25 30  
 Phe Ala Glu Trp Gln Arg Lys Ile Gln Val Leu Ala Asp Gln Lys  
 35 40 45  
 Glu Gly Val Ser Gly Cys Val Thr Pro Thr Glu Ser Leu Ala Ser Leu  
 50 55 60  
 Cys Thr Thr Gln Ser Glu Ile Thr Asp Leu Ser Ser Ala Ser Cys Leu  
 65 70 75 80

```

Arg Gly Phe Met Pro Glu Lys Leu Gln Ile Val Lys Pro Leu Glu Gly
      85          90          95
Ser Gln Thr Leu Tyr His Trp Gln Gln Leu Ala Gln Pro Asn Leu Gly
      100        105        110
Thr Ile Leu Asp Pro Arg Pro Gly Val Ile Thr Lys Gly Phe Thr Gln
      115        120        125
Leu Pro Gly Asp Ala Ile Tyr His Ile Ser Asp Leu Glu Glu Asp Glu
      130        135        140
Glu Glu Gly Ile Thr Phe Gln Val Gln Gln Pro Leu Glu Val Glu Glu
      145        150        155        160
Lys Leu Ser Thr Ser Lys Pro Val Thr Gly Ile Phe Leu Pro Pro Ile
      165        170        175
Thr Ser Ala Gly Gly Pro Val Thr Val Ala Thr Ala Asn Pro Gly Lys
      180        185        190
Cys Leu Ser Cys Thr Asn Ser Thr Phe Thr Phe Thr Thr Cys Arg Ile
      195        200        205
Leu His Pro Ser Asp Ile Thr Gln Val Thr Pro Ser Ser Gly Phe Pro
      210        215        220
Ser Leu Ser Cys Gly Ser Ser Gly Ser Ser Ser Ser Asn Thr Ala Val
      225        230        235        240
Asn Ser Pro Ala Leu Ser Tyr Arg Leu Ser Ile Gly Glu Ser Ile Thr
      245        250        255
Asn Arg Arg Asp Ser Thr Thr Thr Phe Ser Ser Thr Met Ser Leu Ala
      260        265        270
Lys Leu Leu Gln Glu Arg Gly Ile Ser Ala Lys Val Tyr His Ser Pro
      275        280        285
Ile Ser Glu Asn Pro Leu Gln Pro Leu Pro Lys Ser Leu Ala Ile Pro
      290        295        300
Ser Thr Pro Pro Asn Ser Pro Ser His Ser Pro Cys Pro Ser Pro Leu
      305        310        315        320
Pro Phe Glu Pro Arg Val His Leu Ser Glu Asn Phe Leu Ala Ser Arg
      325        330        335
Pro Ala Glu Thr Phe Leu Gln Glu Met Tyr Gly Leu Arg Pro Ser Arg
      340        345        350
Asn Pro Pro Asp Val Gly Gln Leu Lys Met Asn Leu Val Asp Arg Leu
      355        360        365
Lys Arg Leu Gly Ile Ala Arg Val Val Lys Asn Pro Gly Ala Gln Glu
      370        375        380
Asn Gly Arg Cys Gln Glu Ala Glu Ile Gly Pro Gln Lys Pro Asp Ser
      385        390        395        400
Ala Val Tyr Leu Asn Ser Gly Ser Ser Leu Leu Gly Gly Leu Arg Arg
      405        410        415
Asn Gln Ser Leu Pro Val Ile Met Gly Ser Phe Ala Ala Pro Val Cys
      420        425        430
Thr Ser Ser Pro Lys Met Gly Val Leu Lys Glu Asp
      435        440        444

```

<210> 156  
 <211> 145  
 <212> PRT  
 <213> Homo sapiens

```

<400> 156
Met Pro Ser Arg Val Met Pro Met Ala Val Glu Ala Gly Gln Asn Arg
  1          5          10          15
Arg Gln Pro Ala Pro Gln Glu Ala Gly Cys Gly Pro Arg Ala Val Leu
      20        25        30
Asp Gln Ser Asp Val Tyr Thr His Val Leu Ser Ala Phe Arg Gly Lys
      35        40        45
Gly Arg Arg Cys Leu Ile Lys Phe Gly Asp Ser Arg Ala Asp Gly Ile
      50        55        60

```

```

His Ser Val Ser Leu Thr Ser Phe Gln Ile Ala Val Gln His Tyr Leu
 65              70              75              80
His Gly Thr Cys Tyr Gln Asn Pro Cys Pro Ala His Pro Leu Leu Ile
      85              90              95
Cys Trp His Gln Phe Pro Ala Val Pro Arg Pro Gln Arg Leu Gln Thr
      100              105              110
Phe Gly Leu Ser Ala Val Ile Pro Arg Glu Leu Leu Ser Ser Cys Ser
      115              120              125
Ser Ala Ile Ser Gly His Ala Glu Ala Thr Phe Asn Lys Gln Met Met
 130              135              140
Lys
145

```

```

<210> 157
<211> 275
<212> PRT
<213> Homo sapiens

```

```

<400> 157
Met Glu Ser Tyr Ser Val Thr Gln Ala Gly Val Gln Trp His Glu Leu
 1              5              10              15
Cys Ser Leu Gln Pro Ser Pro Pro Arg Phe Arg Glu Met Cys Ile Glu
      20              25              30
Gln Asp Gly Arg Val His Leu Thr Val Val Tyr Phe Gly Lys Glu Glu
      35              40              45
Ile Asn Glu Val Lys Gly Val Leu Glu Asn Thr Ser Lys Ala Ala Asn
      50              55              60
Phe Arg Asn Phe Thr Phe Ile Gln Leu Asn Gly Glu Phe Ser Arg Gly
      65              70              75              80
Lys Gly Leu Asp Val Gly Ala Arg Phe Trp Lys Gly Ser Asn Val Leu
      85              90              95
Leu Phe Phe Cys Asp Val Asp Ile Tyr Phe Thr Ser Glu Phe Leu Asn
      100              105              110
Thr Cys Arg Leu Asn Thr Gln Pro Gly Lys Lys Val Phe Tyr Pro Val
      115              120              125
Leu Phe Ser Gln Tyr Asn Pro Gly Ile Ile Tyr Gly His His Asp Ala
      130              135              140
Val Pro Pro Leu Glu Gln Gln Leu Val Ile Lys Lys Glu Thr Gly Phe
      145              150              155              160
Trp Arg Asp Phe Gly Phe Gly Met Thr Cys Gln Tyr Arg Ser Asp Phe
      165              170              175
Ile Asn Ile Gly Gly Phe Asp Leu Asp Ile Lys Gly Trp Gly Gly Glu
      180              185              190
Asp Val His Leu Tyr Arg Lys Tyr Leu His Ser Asn Leu Ile Val Val
      195              200              205
Arg Thr Pro Val Arg Gly Leu Phe His Leu Trp His Glu Lys Arg Cys
      210              215              220
Met Asp Glu Leu Thr Pro Glu Gln Tyr Lys Met Cys Met Gln Ser Lys
      225              230              235              240
Ala Met Asn Glu Ala Ser His Gly Gln Leu Gly Met Leu Val Phe Arg
      245              250              255
His Glu Ile Glu Ala His Leu Arg Lys Gln Lys Gln Lys Thr Ser Ser
      260              265              270
Lys Lys Thr
      275

```

```

<210> 158
<211> 86
<212> PRT
<213> Homo sapiens

```

&lt;400&gt; 158

```

Met Lys Leu Glu Val Ala Asn Lys Asn Asn Pro Asp Thr Tyr Trp Val
 1          5          10          15
Ala Thr Ile Ile Thr Thr Cys Gly Gln Leu Leu Leu Arg Tyr Cys
          20          25          30
Gly Tyr Gly Glu Asp Arg Arg Ala Asp Phe Trp Cys Asp Val Val Ile
          35          40          45
Ala Asp Leu His Pro Val Gly Trp Cys Thr Gln Asn Asn Lys Val Leu
          50          55          60
Met Pro Pro Asp Asp Val Arg Ala Gly Ala Asp Asn Gly Ala Lys Leu
 65          70          75          80
Gly Phe Ser Glu Leu Lys
          85 86

```

&lt;210&gt; 159

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 159

```

Met Val Glu Leu Val Leu Lys Gln Gly Gln Ser Ser His Trp Val Tyr
 1          5          10          15
Pro Glu Val Gln Ala Val Gly Leu Thr Ile Val Ser Lys Val Gly Trp
          20          25          30
Pro Ile Pro Leu Asp Glu Lys Ile Gln Lys Leu
          35          40          43

```

&lt;210&gt; 160

&lt;211&gt; 45

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 160

```

Met Asn Ile Thr Arg Leu Asn Ile Leu Leu Ala Cys Ser Lys Ile Val
 1          5          10          15
Ser Asn Arg Leu Ile Thr Pro Cys Lys Tyr Gly Ser Ile Phe Val Gly
          20          25          30
Val Ala Ser Phe His Ile His Tyr Ser Phe Ile Leu Val
          35          40          45

```

&lt;210&gt; 161

&lt;211&gt; 719

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

```

Met Lys Pro Pro Ala His Trp Thr Gly Gly Leu Gln Pro Glu Leu Gln
 1          5          10          15
Gly Ser Pro Ala Gly Trp Asp Ser Thr Glu Gly Trp Thr Trp Gly Asp
          20          25          30
Gly Glu His Gly Leu Gly Ala Ala Met Pro Thr Trp Gly Ala Arg
          35          40          45
Pro Ala Ser Pro Asp Arg Phe Ala Val Ser Ala Glu Ala Glu Asn Lys
          50          55          60
Val Arg Glu Gln Gln Pro His Val Glu Arg Ile Phe Ser Val Gly Val

```

65					70					75				80	
Ser	Val	Leu	Pro	Lys	Asp	Cys	Pro	Asp	Asn	Pro	His	Ile	Trp	Leu	Gln
				85					90					95	
Leu	Glu	Gly	Pro	Lys	Glu	Asn	Ala	Ser	Arg	Ala	Lys	Glu	Tyr	Leu	Lys
			100					105					110		
Gly	Leu	Cys	Ser	Pro	Glu	Leu	Gln	Asp	Glu	Ile	His	Tyr	Pro	Pro	Lys
		115					120					125			
Leu	His	Cys	Ile	Phe	Leu	Gly	Ala	Gln	Gly	Phe	Phe	Leu	Asp	Cys	Leu
	130						135				140				
Ala	Trp	Ser	Thr	Ser	Ala	His	Leu	Val	Pro	Arg	Ala	Pro	Gly	Ser	Leu
	145				150					155					160
Met	Ile	Ser	Gly	Leu	Thr	Glu	Ala	Phe	Val	Met	Ala	Gln	Ser	Arg	Val
			165						170					175	
Glu	Glu	Leu	Ala	Glu	Arg	Leu	Ser	Trp	Asp	Phe	Thr	Pro	Gly	Pro	Ser
			180					185					190		
Ser	Gly	Ala	Ser	Gln	Cys	Thr	Gly	Val	Leu	Arg	Asp	Phe	Ser	Ala	Leu
		195					200					205			
Leu	Gln	Ser	Pro	Gly	Asp	Ala	His	Arg	Glu	Ala	Leu	Leu	Gln	Leu	Pro
	210						215				220				
Leu	Ala	Val	Gln	Glu	Glu	Leu	Leu	Ser	Leu	Val	Gln	Glu	Ala	Ser	Ser
	225				230					235					240
Gly	Gln	Gly	Pro	Gly	Ala	Leu	Ala	Ser	Trp	Glu	Gly	Arg	Ser	Ser	Ala
				245					250					255	
Leu	Leu	Gly	Ala	Gln	Cys	Gln	Gly	Val	Arg	Ala	Pro	Pro	Ser	Asp	Gly
		260						265					270		
Arg	Glu	Ser	Leu	Asp	Thr	Gly	Ser	Met	Gly	Pro	Gly	Asp	Cys	Arg	Gly
		275					280					285			
Ala	Arg	Gly	Asp	Thr	Tyr	Ala	Val	Glu	Lys	Glu	Gly	Gly	Thr	Gln	Gly
	290					295					300				
Gly	Pro	Arg	Glu	Met	Asp	Leu	Gly	Trp	Lys	Glu	Leu	Pro	Gly	Glu	Glu
	305				310					315					320
Ala	Trp	Glu	Arg	Glu	Val	Ala	Leu	Arg	Pro	Gln	Ser	Val	Gly	Gly	Gly
			325						330					335	
Ala	Arg	Glu	Ser	Ala	Pro	Leu	Lys	Gly	Lys	Ala	Leu	Gly	Lys	Glu	Glu
			340					345					350		
Ile	Ala	Leu	Gly	Gly	Gly	Gly	Phe	Cys	Val	His	Arg	Glu	Pro	Pro	Gly
		355					360					365			
Ala	His	Gly	Ser	Cys	His	Arg	Ala	Ala	Gln	Ser	Arg	Gly	Ala	Ser	Leu
	370					375					380				
Leu	Gln	Arg	Leu	His	Asn	Gly	Asn	Ala	Ser	Pro	Pro	Arg	Val	Pro	Ser
	385				390					395					400
Pro	Pro	Pro	Ala	Pro	Glu	Pro	Pro	Trp	His	Cys	Gly	Asp	Arg	Gly	Asp
				405					410					415	
Cys	Gly	Asp	Arg	Gly	Asp	Val	Gly	Asp	Arg	Gly	Asp	Lys	Gln	Gln	Gly
			420					425					430		
Met	Ala	Arg	Gly	Arg	Gly	Pro	Gln	Trp	Lys	Arg	Gly	Ala	Arg	Gly	Gly
		435					440					445			
Asn	Leu	Val	Thr	Gly	Thr	Gln	Arg	Phe	Lys	Glu	Ala	Leu	Gln	Asp	Pro
	450					455					460				
Phe	Thr	Leu	Cys	Leu	Ala	Asn	Val	Pro	Gly	Gln	Pro	Asp	Leu	Arg	His
	465				470					475					480
Ile	Val	Ile	Asp	Gly	Ser	Asn	Val	Ala	Met	Val	His	Gly	Leu	Gln	His
			485					490					495		
Tyr	Phe	Ser	Ser	Arg	Gly	Ile	Ala	Ile	Ala	Val	Gln	Tyr	Phe	Trp	Asp
			500					505					510		
Arg	Gly	His	Arg	Asp	Ile	Thr	Val	Phe	Val	Pro	Gln	Trp	Arg	Phe	Ser
		515					520					525			
Lys	Asp	Ala	Lys	Val	Arg	Glu	Ser	His	Phe	Leu	Gln	Lys	Leu	Tyr	Ser
		530					535					540			
Leu	Ser	Leu	Leu	Ser	Leu	Thr	Pro	Ser	Arg	Val	Met	Asp	Gly	Lys	Arg
	545				550					555					560
Ile	Ser	Ser	Tyr	Asp	Asp	Arg	Phe	Met	Val	Lys	Leu	Ala	Glu	Glu	Thr
			565						570					575	

Asp Gly Ile Ile Val Ser Asn Asp Gln Phe Arg Asp Leu Ala Glu Glu  
 580 585 590  
 Ser Glu Lys Trp Met Ala Ile Ile Arg Glu Arg Leu Leu Pro Phe Thr  
 595 600 605  
 Phe Val Gly Asn Leu Phe Met Val Pro Asp Asp Pro Leu Gly Arg Asn  
 610 615 620  
 Gly Pro Thr Leu Asp Glu Phe Leu Lys Lys Pro Ala Arg Thr Gln Gly  
 625 630 635 640  
 Ser Ser Lys Ala Gln His Pro Ser Arg Gly Phe Ala Glu His Gly Lys  
 645 650 655  
 Gln Gln Gln Gly Arg Glu Glu Glu Lys Gly Ser Gly Gly Ile Arg Lys  
 660 665 670  
 Thr Arg Glu Thr Glu Arg Leu Arg Arg Gln Leu Leu Glu Val Phe Trp  
 675 680 685  
 Gly Gln Asp His Lys Val Asp Phe Ile Leu Gln Arg Glu Pro Tyr Cys  
 690 695 700  
 Arg Asp Ile Asn Gln Leu Ser Glu Ala Leu Leu Ser Leu Asn Phe  
 705 710 715 719

<210> 162  
 <211> 747  
 <212> PRT  
 <213> Homo sapiens

<400> 162  
 Met Trp Gly Phe Leu Lys Arg Pro Val Val Val Thr Ala Asp Ile Asn  
 1 5 10 15  
 Leu Ser Leu Val Ala Leu Thr Gly Met Gly Leu Leu Ser Arg Leu Trp  
 20 25 30  
 Arg Leu Thr Tyr Pro Arg Ala Val Phe Asp Glu Val Tyr Tyr Gly  
 35 40 45  
 Gln Tyr Ile Ser Phe Tyr Met Lys Gln Ile Phe Phe Leu Asp Asp Ser  
 50 55 60  
 Gly Pro Pro Phe Gly His Met Val Leu Ala Leu Gly Gly Tyr Leu Gly  
 65 70 75 80  
 Gly Phe Asp Gly Asn Phe Leu Trp Asn Arg Ile Gly Ala Glu Tyr Ser  
 85 90 95  
 Ser Asn Val Pro Val Trp Ser Leu Arg Leu Leu Pro Ala Leu Ala Gly  
 100 105 110  
 Ala Leu Ser Val Pro Met Ala Tyr Gln Ile Val Leu Glu Leu His Phe  
 115 120 125  
 Ser His Cys Ala Ala Met Gly Ala Ala Leu Leu Met Leu Ile Glu Asn  
 130 135 140  
 Ala Leu Ile Thr Gln Ser Arg Leu Met Leu Leu Glu Ser Val Leu Ile  
 145 150 155 160  
 Phe Phe Asn Leu Leu Ala Val Leu Ser Tyr Leu Lys Phe Phe Asn Cys  
 165 170 175  
 Gln Lys His Ser Pro Phe Ser Leu Ser Trp Trp Phe Trp Leu Thr Leu  
 180 185 190  
 Thr Gly Val Ala Cys Ser Cys Ala Val Gly Ile Lys Tyr Met Gly Val  
 195 200 205  
 Phe Thr Tyr Val Leu Val Leu Gly Val Ala Ala Val His Ala Trp His  
 210 215 220  
 Leu Leu Gly Asp Gln Thr Leu Ser Asn Val Gly Ala Asp Val Gln Cys  
 225 230 235 240  
 Cys Met Arg Pro Ala Cys Met Gly Gln Met Arg Met Ser Gln Gly Val  
 245 250 255  
 Cys Val Phe Cys His Leu Leu Ala Arg Ala Val Ala Leu Leu Val Ile  
 260 265 270  
 Pro Val Val Leu Tyr Leu Leu Phe Phe Tyr Val His Leu Ile Leu Val  
 275 280 285



Phe Arg Ser Gly Pro His Asp Gln Ile Met Ser Ser Ala Phe Gln Ala  
 290 295 300  
 Ser Leu Glu Gly Gly Leu Ala Arg Ile Thr Gln Gly Gln Pro Leu Glu  
 305 310 315 320  
 Val Ala Phe Gly Ser Gln Val Thr Leu Arg Asn Val Phe Gly Lys Pro  
 325 330 335  
 Val Pro Cys Trp Leu His Ser His Gln Asp Thr Tyr Pro Met Ile Tyr  
 340 345 350  
 Glu Asn Gly Arg Gly Ser Ser His Gln Gln Gln Val Thr Cys Tyr Pro  
 355 360 365  
 Phe Lys Asp Val Asn Asn Trp Trp Ile Val Lys Asp Pro Arg Arg His  
 370 375 380  
 Gln Leu Val Val Ser Ser Pro Pro Arg Pro Val Arg His Gly Asp Met  
 385 390 395 400  
 Val Gln Leu Val His Gly Met Thr Thr Arg Ser Leu Asn Thr His Asp  
 405 410 415  
 Val Ala Ala Pro Leu Ser Pro His Ser Gln Glu Val Ser Cys Tyr Ile  
 420 425 430  
 Asp Tyr Asn Ile Ser Met Pro Ala Gln Asn Leu Trp Arg Leu Glu Ile  
 435 440 445  
 Val Asn Arg Gly Ser Asp Thr Asp Val Trp Lys Thr Ile Leu Ser Glu  
 450 455 460  
 Val Arg Phe Val His Val Asn Thr Ser Ala Val Leu Lys Leu Ser Gly  
 465 470 475 480  
 Ala His Leu Pro Asp Trp Gly Tyr Arg Gln Leu Glu Ile Val Gly Glu  
 485 490 495  
 Lys Leu Ser Arg Gly Tyr His Gly Ser Thr Val Trp Asn Val Glu Glu  
 500 505 510  
 His Arg Tyr Gly Ala Ser Gln Glu Gln Arg Glu Arg Glu Arg Glu Leu  
 515 520 525  
 His Ser Pro Ala Gln Val Asp Val Ser Arg Asn Leu Ser Phe Met Ala  
 530 535 540  
 Arg Phe Ser Glu Leu Gln Trp Arg Met Leu Ala Leu Arg Ser Asp Asp  
 545 550 555 560  
 Ser Glu His Lys Tyr Ser Ser Ser Pro Leu Glu Trp Val Thr Leu Asp  
 565 570 575  
 Thr Asn Ile Ala Tyr Trp Leu His Pro Arg Thr Ser Ala Gln Ile His  
 580 585 590  
 Leu Leu Gly Asn Ile Val Ile Trp Val Ser Gly Ser Leu Ala Leu Ala  
 595 600 605  
 Ile Tyr Ala Leu Leu Ser Leu Trp Tyr Leu Leu Arg Arg Arg Arg Asn  
 610 615 620  
 Val His Asp Leu Pro Gln Asp Ala Trp Leu Arg Trp Val Leu Ala Gly  
 625 630 635 640  
 Ala Leu Cys Ala Gly Gly Trp Ala Val Asn Tyr Leu Pro Phe Phe Leu  
 645 650 655  
 Met Glu Lys Thr Leu Phe Leu Tyr His Tyr Leu Pro Ala Leu Thr Phe  
 660 665 670  
 Gln Ile Leu Leu Leu Pro Val Val Leu Gln His Ile Ser Asp His Leu  
 675 680 685  
 Cys Arg Ser Gln Leu Gln Arg Ser Ile Phe Ser Ala Leu Val Val Ala  
 690 695 700  
 Trp Tyr Ser Ser Ala Cys His Val Ser Asn Thr Leu Arg Pro Leu Thr  
 705 710 715 720  
 Tyr Gly Asp Lys Ser Leu Ser Pro His Glu Leu Lys Ala Leu Arg Trp  
 725 730 735  
 Lys Asp Ser Trp Asp Ile Leu Ile Arg Lys His  
 740 745 747

&lt;210&gt; 163

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 163

```

Met Tyr Glu Gly Lys Glu Asn Val Ser Phe Glu Leu Gln Arg Asp Phe
 1      5      10      15
Ser Gln Glu Thr Asp Phe Ser Glu Ala Ser Leu Leu Glu Lys Gln Gln
      20      25      30
Glu Val His Ser Ala Gly Asn Ile Lys Lys Glu Lys Ser Asn Thr Ile
      35      40      45
Asp Gly Thr Val Lys Asp Glu Thr Ser Pro Val Glu Glu Cys Phe Phe
      50      55      60
Ser Gln Ser Ser Asn Ser Tyr Gln Cys His Thr Ile Thr Gly Glu Gln
      65      70      75      80
Pro Ser Gly Cys Thr Gly Leu Gly Lys Ser Ile Ser Phe Asp Thr Lys
      85      90      95
Leu Val Lys His Glu Ile Ile Asn Ser Glu Glu Arg Pro Phe Lys Cys
      100      105      110
Glu Glu Leu Val Glu Pro Phe Arg Cys Asp Ser Gln Leu Ile Gln His
      115      120      125
Gln Glu Asn Asn Thr Glu Glu Lys Pro Tyr Gln Cys Ser Glu Cys Gly
      130      135      140
Lys Ala Phe Ser Ile Asn Glu Lys Leu Ile Trp His Gln Arg Leu His
      145      150      155      160
Ser Gly Glu Lys Pro Phe Lys Cys Val Glu Cys Gly Lys Ser Phe Ser
      165      170      175
Tyr Ser Ser His Tyr Ile Thr His His Ile Asn Phe Gln Trp Gly Arg
      180      185      190
Ala Pro Ile Ile Val Arg Cys Val Gly Arg Pro Ser Met Leu Met Glu
      195      200      205
Ala
209

```

&lt;210&gt; 164

&lt;211&gt; 699

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 164

```

Met Ala Pro Leu Lys Val Trp Gln Leu Gln Asp Leu Ser Phe Gln Thr
 1      5      10      15
Ala Ala Arg Ile Leu Ala Ser Pro Val Glu Leu Ala Leu Val Val Met
      20      25      30
Lys Asp Leu Ser Gln Asn Phe Pro Thr Lys Ala Arg Ala Ile Thr Lys
      35      40      45
Thr Ala Val Ser Ser Glu Leu Arg Thr Glu Val Glu Glu Asn Gln Lys
      50      55      60
Tyr Phe Lys Gly Thr Leu Gly Leu Gln Pro Gly Asp Ser Ala Leu Phe
      65      70      75      80
Ile Asn Gly Leu His Met Asp Leu Asp Thr Gln Asp Ile Phe Ser Leu
      85      90      95
Phe Asp Val Leu Arg Asn Glu Ala Arg Val Met Glu Gly Leu His Arg
      100      105      110
Leu Gly Ile Glu Gly Leu Ser Leu His Asn Val Leu Lys Leu Asn Ile
      115      120      125
Gln Pro Ser Glu Ala Asp Tyr Ala Val Asp Ile Arg Ser Pro Ala Ile
      130      135      140
Ser Trp Val Asn Asn Leu Glu Val Asp Ser Arg Tyr Asn Ser Trp Pro
      145      150      155      160
Ser Ser Leu Gln Glu Leu Leu Arg Pro Thr Phe Pro Gly Val Ile Arg
      165      170      175

```

Gln Ile Arg Lys Asn Leu His Asn Met Val Phe Ile Val Asp Pro Ala  
 180 185 190  
 His Glu Thr Thr Ala Glu Leu Met Asn Thr Ala Glu Met Phe Leu Ser  
 195 200 205  
 Asn His Ile Pro Leu Arg Ile Gly Phe Ile Phe Val Val Asn Asp Ser  
 210 215 220  
 Glu Asp Val Asp Gly Met Gln Asp Ala Gly Val Ala Val Leu Arg Ala  
 225 230 235 240  
 Tyr Asn Tyr Val Ala Gln Glu Val Asp Asp Tyr His Ala Phe Gln Thr  
 245 250 255  
 Leu Thr His Ile Tyr Asn Lys Val Arg Thr Gly Glu Lys Val Lys Val  
 260 265 270  
 Glu His Val Val Ser Val Leu Glu Lys Lys Tyr Pro Tyr Val Glu Val  
 275 280 285  
 Asn Ser Ile Leu Gly Ile Asp Ser Ala Tyr Asp Arg Asn Arg Lys Glu  
 290 295 300  
 Ala Arg Gly Tyr Tyr Glu Gln Thr Gly Val Gly Pro Leu Pro Val Val  
 305 310 315 320  
 Leu Phe Asn Gly Met Pro Phe Glu Arg Glu Gln Leu Asp Pro Asp Glu  
 325 330 335  
 Leu Glu Thr Ile Thr Met His Lys Ile Leu Glu Thr Thr Thr Phe Phe  
 340 345 350  
 Gln Arg Ala Val Tyr Leu Gly Glu Leu Pro His Asp Gln Asp Val Val  
 355 360 365  
 Glu Tyr Ile Met Asn Gln Pro Asn Val Val Pro Arg Ile Asn Ser Arg  
 370 375 380  
 Ile Leu Thr Ala Glu Arg Asp Tyr Leu Asp Leu Thr Ala Ser Asn Asn  
 385 390 395 400  
 Phe Phe Val Asp Asp Tyr Ala Arg Phe Thr Ile Leu Asp Ser Gln Gly  
 405 410 415  
 Lys Thr Ala Ala Val Ala Asn Ser Met Asn Tyr Leu Thr Lys Lys Gly  
 420 425 430  
 Met Ser Ser Lys Glu Ile Tyr Asp Asp Ser Phe Ile Arg Pro Val Thr  
 435 440 445  
 Phe Trp Ile Val Gly Asp Phe Asp Ser Pro Ser Gly Arg Gln Leu Leu  
 450 455 460  
 Tyr Asp Ala Ile Lys His Gln Lys Ser Ser Asn Asn Val Arg Ile Ser  
 465 470 475 480  
 Met Ile Asn Asn Pro Ala Lys Glu Ile Ser Tyr Glu Asn Thr Gln Ile  
 485 490 495  
 Ser Arg Ala Ile Trp Ala Ala Leu Gln Thr Gln Thr Ser Asn Ala Ala  
 500 505 510  
 Lys Asn Phe Ile Thr Lys Met Ala Lys Glu Gly Ala Ala Glu Ala Leu  
 515 520 525  
 Ala Ala Gly Ala Asp Ile Ala Glu Phe Ser Val Gly Gly Met Asp Phe  
 530 535 540  
 Ser Leu Phe Lys Glu Val Phe Glu Ser Ser Lys Met Asp Phe Ile Leu  
 545 550 555 560  
 Ser His Ala Val Tyr Cys Arg Asp Val Leu Lys Leu Lys Lys Gly Gln  
 565 570 575  
 Arg Ala Val Ile Ser Asn Gly Arg Ile Ile Gly Pro Leu Glu Asp Ser  
 580 585 590  
 Glu Leu Phe Asn Gln Asp Asp Phe His Leu Leu Glu Asn Ile Ile Leu  
 595 600 605  
 Lys Thr Ser Gly Gln Lys Ile Lys Ser His Ile Gln Gln Leu Arg Val  
 610 615 620  
 Glu Glu Asp Val Ala Ser Asp Leu Val Met Lys Val Asp Ala Leu Leu  
 625 630 635 640  
 Ser Ala Gln Pro Lys Gly Asp Pro Arg Ile Glu Tyr Gln Phe Phe Glu  
 645 650 655  
 Asp Arg His Ser Ala Ile Lys Leu Arg Pro Lys Glu Gly Glu Thr Tyr  
 660 665 670  
 Phe Asp Val Val Ala Val Val Asp Pro Val Thr Arg Glu Ala Gln Arg

675                      680                      685  
 Leu Ala Pro Leu Ala Leu Gly Phe Gly Leu Ser  
 690                      695                      699

<210> 165  
 <211> 194  
 <212> PRT  
 <213> Homo sapiens

<400> 165  
 Met Gly Ile Ile Gln Arg Ala Met Val Lys Ala Cys Pro His Val Trp  
 1                      5                      10                      15  
 Phe Glu Arg Ser Glu Met Lys Asp Arg His Leu Val Thr Lys Arg Leu  
 20                      25                      30  
 Lys Glu His Ile Ala Asp Lys Lys Lys Leu Pro Ile Leu Ile Phe Pro  
 35                      40                      45  
 Glu Gly Thr Cys Ile Asn Asn Thr Ser Val Met Met Phe Lys Lys Gly  
 50                      55                      60  
 Ser Phe Glu Ile Gly Gly Thr Ile His Pro Val Ala Ile Lys Tyr Asn  
 65                      70                      75                      80  
 Pro Gln Phe Gly Asp Ala Phe Trp Asn Ser Ser Lys Tyr Asn Met Val  
 85                      90                      95  
 Ser Tyr Leu Leu Arg Met Met Thr Ser Trp Ala Ile Val Cys Asp Val  
 100                      105                      110  
 Trp Tyr Met Pro Pro Met Thr Arg Glu Glu Gly Glu Asp Ala Val Gln  
 115                      120                      125  
 Phe Ala Asn Arg Val Lys Ser Ala Ile Ala Ile Gln Gly Gly Leu Thr  
 130                      135                      140  
 Glu Leu Pro Trp Asp Gly Gly Leu Lys Arg Ala Lys Val Lys Asp Ile  
 145                      150                      155                      160  
 Phe Lys Glu Glu Gln Leu Ile Ile Leu Gln Gln Asp Asp Cys Gly Gln  
 165                      170                      175  
 Trp Ile Ser Gln Leu Arg Gly Arg Met Thr Ala Phe Ile Ser Arg Thr  
 180                      185                      190  
 Ser Pro  
 194

<210> 166  
 <211> 1080  
 <212> PRT  
 <213> Homo sapiens

<400> 166  
 Met Ala Glu Ser Ser Pro Thr Asn Ser Pro Ser Ser Gly Asn His Leu  
 1                      5                      10                      15  
 Ala Thr Pro Gln Arg Pro Asp Gln Thr Val Thr Asn Gly Gln Asp Ser  
 20                      25                      30  
 Pro Ala Ser Leu Leu Asn Ile Ser Ala Gly Ser Asp Asp Ser Val Phe  
 35                      40                      45  
 Asp Ser Ser Ser Asp Met Glu Lys Phe Thr Glu Ile Ile Lys Gln Met  
 50                      55                      60  
 Asp Ser Ala Val Cys Met Pro Met Lys Arg Lys Lys Ala Arg Met Pro  
 65                      70                      75                      80  
 Asn Ser Pro Ala Pro His Phe Ala Met Pro Pro Ile His Glu Asp His  
 85                      90                      95  
 Leu Glu Lys Val Phe Asp Pro Lys Val Phe Thr Phe Gly Leu Gly Lys  
 100                      105                      110  
 Lys Lys Glu Ser Gln Pro Glu Met Ser Pro Ala Leu His Leu Met Gln  
 115                      120                      125

Asn	Leu	Asp	Thr	Lys	Ser	Lys	Leu	Arg	Pro	Lys	Arg	Ala	Ser	Ala	Glu
130						135					140				
Gln	Ser	Val	Leu	Phe	Lys	Ser	Leu	His	Thr	Asn	Thr	Asn	Gly	Asn	Ser
145					150					155					160
Glu	Pro	Leu	Val	Met	Pro	Glu	Ile	Asn	Asp	Lys	Glu	Asn	Arg	Asp	Val
				165					170					175	
Thr	Asn	Gly	Gly	Ile	Lys	Arg	Ser	Arg	Leu	Glu	Lys	Ser	Ala	Leu	Phe
			180					185					190		
Ser	Ser	Leu	Leu	Ser	Ser	Leu	Pro	Gln	Asp	Lys	Ile	Phe	Ser	Pro	Ser
		195					200					205			
Val	Thr	Ser	Val	Asn	Thr	Met	Thr	Thr	Ala	Phe	Ser	Thr	Ser	Gln	Asn
	210					215						220			
Gly	Ser	Leu	Ser	Gln	Ser	Ser	Val	Ser	Gln	Pro	Thr	Thr	Glu	Gly	Ala
225					230					235					240
Pro	Pro	Cys	Gly	Leu	Asn	Lys	Glu	Gln	Ser	Asn	Leu	Leu	Pro	Asp	Asn
				245					250					255	
Ser	Leu	Lys	Val	Phe	Asn	Phe	Asn	Ser	Ser	Ser	Thr	Ser	His	Ser	Ser
			260					265					270		
Leu	Lys	Ser	Pro	Ser	His	Met	Glu	Lys	Tyr	Pro	Gln	Lys	Glu	Lys	Thr
	275						280					285			
Lys	Glu	Asp	Leu	Asp	Ser	Arg	Ser	Asn	Leu	His	Leu	Pro	Glu	Thr	Lys
	290					295					300				
Phe	Ser	Glu	Leu	Ser	Lys	Leu	Lys	Asn	Asp	Asp	Met	Glu	Lys	Ala	Asn
305					310					315					320
His	Ile	Glu	Ser	Val	Ile	Lys	Ser	Asn	Leu	Pro	Asn	Cys	Ala	Asn	Ser
				325					330					335	
Asp	Thr	Asp	Phe	Met	Gly	Leu	Phe	Lys	Ser	Ser	Arg	Tyr	Asp	Pro	Ser
			340					345					350		
Ile	Ser	Phe	Ser	Gly	Met	Ser	Leu	Ser	Asp	Thr	Met	Thr	Leu	Arg	Gly
		355					360					365			
Ser	Val	Gln	Asn	Lys	Leu	Asn	Pro	Arg	Pro	Gly	Lys	Val	Val	Ile	Tyr
	370					375					380				
Ser	Glu	Pro	Asp	Val	Ser	Glu	Lys	Cys	Ile	Glu	Val	Phe	Ser	Asp	Ile
385					390					395					400
Gln	Asp	Cys	Ser	Ser	Trp	Ser	Leu	Ser	Pro	Val	Ile	Leu	Ile	Lys	Val
				405					410					415	
Val	Arg	Gly	Cys	Trp	Ile	Leu	Tyr	Glu	Gln	Pro	Asn	Phe	Glu	Gly	His
			420					425					430		
Ser	Ile	Pro	Leu	Glu	Glu	Gly	Glu	Leu	Glu	Ser	Gly	Leu	Trp	Gly	
		435					440				445				
Ile	Glu	Asp	Ile	Leu	Glu	Arg	His	Glu	Glu	Ala	Glu	Ser	Asp	Lys	Pro
	450					455					460				
Val	Val	Ile	Gly	Ser	Ile	Arg	His	Val	Val	Gln	Asp	Tyr	Arg	Val	Ser
465					470					475					480
His	Ile	Asp	Leu	Phe	Thr	Glu	Pro	Glu	Gly	Leu	Gly	Ile	Leu	Ser	Ser
			485						490				495		
Tyr	Phe	Asp	Asp	Thr	Glu	Glu	Met	Gln	Gly	Phe	Gly	Val	Met	Gln	Lys
			500					505					510		
Thr	Cys	Ser	Met	Lys	Val	His	Trp	Gly	Thr	Trp	Leu	Ile	Tyr	Glu	Glu
		515					520					525			
Pro	Gly	Phe	Gln	Gly	Val	Pro	Phe	Ile	Leu	Glu	Pro	Gly	Glu	Tyr	Pro
	530					535					540				
Asp	Leu	Ser	Phe	Trp	Asp	Thr	Glu	Ala	Ala	Tyr	Ile	Gly	Ser	Met	Arg
545					550					555					560
Pro	Leu	Lys	Met	Gly	Gly	Arg	Lys	Val	Glu	Phe	Pro	Thr	Asp	Pro	Lys
			565						570				575		
Val	Val	Val	Tyr	Glu	Lys	Pro	Phe	Phe	Glu	Gly	Lys	Cys	Val	Glu	Leu
			580					585					590		
Glu	Thr	Gly	Met	Cys	Ser	Phe	Val	Met	Glu	Gly	Gly	Glu	Thr	Glu	Glu
		595					600					605			
Ala	Thr	Gly	Asp	Asp	His	Leu	Pro	Phe	Thr	Ser	Val	Gly	Ser	Met	Lys
	610					615					620				
Val	Leu	Arg	Gly	Ile	Trp	Val	Ala	Tyr	Glu	Lys	Pro	Gly	Phe	Thr	Gly

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625          630          635          640
His Gln Tyr Leu Leu Glu Glu Gly Glu Tyr Arg Asp Trp Lys Ala Trp
          645          650          655
Gly Gly Tyr Asn Gly Glu Leu Gln Ser Leu Arg Pro Ile Leu Gly Asp
          660          665          670
Phe Ser Asn Ala His Met Ile Met Tyr Ser Glu Lys Asn Phe Gly Ser
          675          680          685
Lys Gly Ser Ser Ile Asp Val Leu Gly Ile Val Ala Asn Leu Lys Glu
          690          695          700
Thr Gly Tyr Gly Val Lys Thr Gln Ser Ile Asn Val Leu Ser Gly Val
705          710          715          720
Trp Val Ala Tyr Glu Asn Pro Asp Phe Thr Gly Glu Gln Tyr Ile Leu
          725          730          735
Asp Lys Gly Phe Tyr Thr Ser Phe Glu Asp Trp Gly Gly Lys Asn Tyr
          740          745          750
Lys Ile Ser Ser Val Gln Pro Ile Cys Leu Asp Ser Phe Thr Gly Pro
          755          760          765
Arg Arg Arg Asn Gln Ile His Leu Phe Ser Glu Pro Gln Phe Gln Gly
770          775          780
His Ser Gln Ser Phe Glu Thr Thr Ser Gln Ile Asp Asp Ser Phe
785          790          795          800
Ser Thr Lys Ser Cys Arg Val Ser Gly Gly Ser Trp Val Val Tyr Asp
          805          810          815
Gly Glu Asn Phe Thr Gly Asn Gln Tyr Val Leu Glu Glu Gly His Tyr
          820          825          830
Pro Cys Leu Ser Ala Met Gly Cys Pro Pro Gly Ala Thr Phe Lys Ser
          835          840          845
Leu Arg Phe Ile Asp Val Glu Phe Ser Glu Pro Thr Ile Ile Leu Phe
          850          855          860
Glu Arg Glu Asp Phe Lys Gly Lys Lys Ile Glu Leu Asn Ala Glu Thr
865          870          875          880
Val Asn Leu Arg Ser Leu Gly Phe Asn Thr Gln Ile Arg Ser Val Gln
          885          890          895
Val Ile Gly Gly Ile Trp Val Thr Tyr Glu Tyr Gly Ser Tyr Arg Gly
          900          905          910
Arg Gln Phe Leu Leu Ser Pro Ala Glu Val Pro Asn Trp Tyr Glu Phe
          915          920          925
Ser Gly Cys Arg Gln Ile Gly Ser Leu Arg Pro Phe Val Gln Lys Arg
930          935          940
Ile Tyr Phe Arg Leu Arg Asn Lys Ala Thr Gly Leu Phe Met Ser Thr
945          950          955          960
Asn Gly Asn Leu Glu Asp Leu Lys Leu Leu Arg Ile Gln Val Met Glu
          965          970          975
Asp Val Gly Ala Asp Asp Gln Ile Trp Ile Tyr Gln Glu Gly Cys Ile
          980          985          990
Lys Cys Arg Ile Ala Glu Asp Cys Cys Leu Thr Ile Val Gly Ser Leu
          995          1000          1005
Val Thr Ser Gly Ser Lys Leu Gly Leu Ala Leu Asp Gln Asn Ala Asp
1010          1015          1020
Ser Gln Phe Trp Ser Leu Lys Ser Asp Gly Arg Ile Tyr Ser Lys Leu
1025          1030          1035          1040
Lys Pro Asn Leu Val Leu Asp Ile Lys Gly Gly Thr Gln Tyr Asp Gln
          1045          1050          1055
Asn His Ile Ile Leu Asn Thr Val Ser Lys Glu Lys Phe Thr Gln Val
          1060          1065          1070
Trp Glu Ala Met Val Leu Tyr Thr
          1075          1080

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<210> 167
<211> 81
<212> PRT
<213> Homo sapiens

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&lt;400&gt; 167

```

Met Met Gly Leu Cys Pro Ser Lys Pro Ile Gly Ser Gln Met His Leu
 1           5           10           15
Ile Pro Leu Thr Gly Thr Pro Gln Leu Ser Leu Arg Pro Pro Leu Asn
           20           25           30
Val Leu Arg Thr Leu Arg Ile Ala His Ser Trp Ala Glu Ser Ser Asn
           35           40           45
Thr Asn Ser Ile Phe Ile Ile Glu Cys Trp Asn Ile Ser Cys Asn Leu
           50           55           60
Leu Asn Ile Val His Tyr Val Glu Asn Cys Gln Pro Ile Pro His Pro
           65           70           75           80
Leu
81

```

&lt;210&gt; 168

&lt;211&gt; 218

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

```

Met Ala Leu Arg Ala Ser Ala Met Cys Ser Lys Ser Lys Val Lys Lys
 1           5           10           15
Ser Met Phe Ser Lys Pro Cys Ser Val Phe Pro Ser Trp Gln Pro Leu
           20           25           30
Glu Ala Ser Thr Met Leu Leu Met Ser Cys Leu Ala Val Lys Arg Lys
           35           40           45
Val Ala Pro Pro Gly Ser Ser Arg Asp Trp Met Ala Val Ser Thr Ser
           50           55           60
Phe Val Asp Leu Ser Ser Cys Ser Trp Tyr Cys Trp Met Arg Ala Ser
           65           70           75           80
Met Lys Ile Ser Phe Phe Ser Cys Ser Cys Glu Ile Arg Ser Ser Asn
           85           90           95
Ser Leu Phe Phe Ser Ser Arg Met Ala Tyr Asn Val Ser Asn Phe Trp
           100          105          110
Leu Ser Ser Ser Ile Tyr Val Val Thr Val Leu Leu Gly His Ser Thr
           115          120          125
Gly Ile Leu Gln Leu Ser Asp Asp Gly Leu His Thr Val Ile Pro Arg
           130          135          140
His Gln His Gly Asp Thr Val Ile Gln Phe Ser Leu Leu Ser Leu Glu
           145          150          155          160
Asp Thr Leu Gln Trp Gly His Leu Ala Gly Leu Val Asp Pro Lys His
           165          170          175
Leu Ala His Gly Ala Gly Gly His Leu Thr Arg Glu Thr Val Asp Val
           180          185          190
Asp Phe Leu Ile Phe Val Leu Leu Ala His Gly Leu Ser Trp Pro Ser
           195          200          205
Ala Ala Ala Asp Trp Lys His Ser Cys Leu
           210          215          218

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&lt;210&gt; 169

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 169

```

Met Leu His Val Leu Ile Lys Arg Met Cys Ile Leu Gln Leu Leu Asp
 1           5           10           15

```

Lys Met Phe Cys Lys Cys Leu Leu Gly Gln Phe Gly Leu Lys Arg Ser  
                   20                  25                  30  
 Phe Asn Pro Met Phe Ile Phe Cys Leu His Asp Leu Ser Asp Ala Asp  
                   35                  40                  45  
 Asn Gly  
       50

<210> 170  
 <211> 140  
 <212> PRT  
 <213> Homo sapiens

<400> 170  
 Met Asn Gly Pro Ile Lys Lys Lys Pro Lys Ile Ile Pro Asp Asp Pro  
   1                  5                  10                  15  
 Ser Trp Val Gly Gln Ala Thr Asn Val Phe Val Asn Met Glu Glu Asp  
                   20                  25                  30  
 Phe Met Lys Pro Val Ile Asn Ile Val Asp Glu Leu Leu Glu Ala Gly  
                   35                  40                  45  
 Ile Asn Val Thr Val Tyr Asn Gly Gln Leu Asp Leu Ile Val His Thr  
                   50                  55                  60  
 Met Gly Gln Glu Ala Trp Val Arg Lys Leu Lys Trp Pro Glu Leu Pro  
   65                  70                  75                  80  
 Lys Phe Ser Gln Leu Lys Trp Lys Ala Leu Tyr Ser Asp Pro Lys Ser  
                   85                  90                  95  
 Leu Glu Thr Ser Ala Phe Val Lys Ser Tyr Lys Asn Leu Ala Phe Tyr  
                   100                  105                  110  
 Trp Ile Leu Lys Ala Gly His Met Val Pro Ser Asp Gln Gly Asp Met  
                   115                  120                  125  
 Ala Leu Lys Met Met Arg Leu Val Thr Gln Gln Glu  
   130                  135                  140

<210> 171  
 <211> 73  
 <212> PRT  
 <213> Homo sapiens

<400> 171  
 Met Gly Cys Gly Ser Ala His Glu Arg Ile Leu Asp Lys Cys Arg Ser  
   1                  5                  10                  15  
 Arg Thr Ala Val Pro Ile Cys Cys Thr Pro His Ile Tyr Leu Ser Phe  
                   20                  25                  30  
 Pro Asp Ser Cys His Ser Lys Asn Glu Leu Lys Lys Gly Leu Gly Gly  
                   35                  40                  45  
 Gly Val Pro Arg Cys Gln Phe Phe Ser Trp Arg Ala Leu Gly Leu Gln  
                   50                  55                  60  
 Gln Tyr Leu Trp Asp Gly Lys Asn Glu  
   65                  70                  73

<210> 172  
 <211> 185  
 <212> PRT  
 <213> Homo sapiens

<400> 172  
 Met Gln Glu Ser Val Ser Pro Pro His Ser Gln Gln Leu Trp Ala Gly  
   1                  5                  10                  15



```

Ile Thr Gly Lys Pro Val Ala Gly Ala Ser Ser Gln Lys Leu His Pro
      20      25      30
Thr His Trp Asn Ala His Gly Trp Gly Pro Phe Leu Thr Asn Ser Leu
      35      40      45
Ile Ser Thr Gly Asp Leu Ala Asn Glu Leu Val Arg His Phe Leu Ile
      50      55      60
Glu Cys Thr Pro Lys Gly Val Arg Leu Lys Gly Cys Ser Asn Glu Pro
      65      70      75      80
Tyr Phe Gly Ser Leu Thr Ala Leu Val Cys Gln His Ser Ile Thr Pro
      85      90      95
Leu Ala Leu Pro Cys Lys Leu Leu Ile Pro Glu Arg Asp Pro Leu Glu
      100      105      110
Glu Ile Ala Glu Ser Ser Pro Gln Thr Ala Ala Asn Ser Ala Ala Glu
      115      120      125
Leu Leu Lys Gln Gly Ala Ala Cys Asn Val Trp Tyr Leu Asn Ser Val
      130      135      140
Glu Met Glu Ser Leu Thr Gly His Gln Ala Ile Gln Lys Ala Leu Ser
      145      150      155      160
Ile Thr Leu Val Gln Glu Pro Pro Pro Cys Val His Ser Cys Ala Leu
      165      170      175
Gln Gly Val Ser Pro Gly His His Arg
      180      185

```

&lt;210&gt; 173

&lt;211&gt; 283

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 173

```

Met Pro Lys Lys His Asn Leu Gly Ile Asn Asn Asn Asn Ile Leu Gln
  1      5      10      15
Pro Val Asp Ser Lys Ile Gln Glu Ile Glu Tyr Met Glu Asn His Ile
      20      25      30
Asn Ser Lys Arg Leu Asn Asn Asp Leu Val Gly Ser Thr Glu Asn Leu
      35      40      45
Leu Lys Glu Asp Ser Cys Thr Ala Ser Ser Lys Asn Tyr Lys Asn Ala
      50      55      60
Ser Gly Val Val Asn Ser Ser Pro Arg Ser His Ser Ala Thr Asn Gly
      65      70      75      80
Ser Ile Pro Ser Ser Ser Ser Lys Asn Glu Lys Lys Gln Lys Cys Thr
      85      90      95
Ser Lys Ser Pro Ser Thr His Lys Asp Leu Met Glu Asn Cys Ile Pro
      100      105      110
Asn Asn Gln Leu Ser Lys Pro Asp Ala Leu Val Arg Leu Glu Gln Asp
      115      120      125
Ile Lys Lys Leu Lys Ala Asp Leu Gln Ala Ser Arg Gln Val Glu Gln
      130      135      140
Glu Leu Arg Ser Gln Ile Ser Ser Leu Ser Ser Thr Glu Arg Gly Ile
      145      150      155      160
Arg Ser Glu Met Gly Gln Leu Arg Gln Glu Asn Glu Leu Leu Gln Asn
      165      170      175
Lys Leu His Asn Ala Val Gln Met Lys Gln Lys Asp Lys Gln Asn Ile
      180      185      190
Ser Gln Leu Glu Lys Lys Leu Lys Ala Glu Gln Glu Ala Arg Ser Phe
      195      200      205
Val Glu Lys Gln Leu Met Glu Glu Lys Lys Arg Lys Lys Leu Glu Glu
      210      215      220
Ala Thr Ala Ala Arg Ala Val Ala Phe Ala Ala Ala Ser Arg Gly Glu
      225      230      235      240
Cys Thr Glu Thr Leu Arg Asn Arg Ile Arg Glu Leu Glu Ala Glu Gly
      245      250      255

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Lys Lys Leu Thr Asp Gly His Glu Gly Glu Arg Arg Pro Asn Gln Arg  
 260 265 270  
 Thr Arg Thr Lys Ser Pro Gly Ala Ser Glu Ile  
 275 280 283

<210> 174  
 <211> 390  
 <212> PRT  
 <213> Homo sapiens

<400> 174  
 Met Glu Asp Leu Thr Asp Glu Glu Glu Val Pro Ala Ser Gln Ser Thr  
 1 5 10 15  
 Glu Asn Arg Val Leu Pro Ala Pro Ala Pro Arg Arg Glu Lys Thr Asn  
 20 25 30  
 Glu Glu Leu Gln Glu Glu Leu Arg Asn Leu Gln Glu Gln Met Lys Ala  
 35 40 45  
 Leu Gln Glu Gln Leu Lys Val Thr Thr Ile Lys Gln Thr Ala Ser Pro  
 50 55 60  
 Ala Arg Leu Gln Lys Ser Pro Glu Lys Ser Pro Arg Pro Pro Leu Lys  
 65 70 75 80  
 Glu Arg Arg Val Gln Arg Ile Gln Glu Ser Thr Cys Phe Ser Ala Glu  
 85 90 95  
 Leu Asp Val Pro Ala Leu Pro Arg Thr Lys Arg Val Ala Arg Thr Pro  
 100 105 110  
 Lys Ala Ser Pro Pro Asp Pro Lys Ser Ser Ser Ser Arg Met Thr Ser  
 115 120 125  
 Ala Pro Ser Gln Pro Leu Gln Thr Ile Ser Arg Asn Lys Pro Ser Gly  
 130 135 140  
 Ile Thr Arg Gly Gln Ile Val Gly Thr Pro Gly Ser Ser Gly Glu Thr  
 145 150 155 160  
 Thr Gln Pro Ile Cys Val Glu Ala Phe Ser Gly Leu Arg Leu Arg Arg  
 165 170 175  
 Pro Arg Val Ser Ser Thr Glu Met Asn Lys Lys Met Thr Gly Arg Lys  
 180 185 190  
 Leu Ile Arg Leu Ser Gln Ile Lys Glu Lys Met Ala Arg Glu Lys Leu  
 195 200 205  
 Glu Glu Ile Asp Trp Val Thr Phe Gly Val Ile Leu Lys Lys Val Thr  
 210 215 220  
 Pro Gln Ser Val Asn Ser Gly Lys Thr Phe Ser Ile Trp Lys Leu Asn  
 225 230 235 240  
 Asp Leu Arg Asp Leu Thr Gln Cys Val Ser Leu Phe Leu Phe Gly Glu  
 245 250 255  
 Val His Lys Ala Leu Trp Lys Thr Glu Gln Gly Thr Val Val Gly Ile  
 260 265 270  
 Leu Asn Ala Asn Pro Met Lys Pro Lys Asp Gly Ser Glu Glu Val Cys  
 275 280 285  
 Leu Ser Ile Asp His Pro Gln Lys Val Leu Ile Met Gly Glu Ala Leu  
 290 295 300  
 Asp Leu Gly Thr Cys Lys Ala Lys Lys Lys Asn Gly Glu Pro Cys Thr  
 305 310 315 320  
 Gln Thr Val Asn Leu Arg Asp Cys Glu Tyr Cys Gln Tyr His Val Gln  
 325 330 335  
 Ala Gln Tyr Lys Lys Leu Ser Ala Lys Arg Ala Asp Leu Gln Ser Thr  
 340 345 350  
 Phe Ser Gly Gly Gln Thr Pro Asn Lys Phe Ala Arg Arg Gly Thr Ser  
 355 360 365  
 Leu Leu Glu Arg Val Cys Gln Asp Gly Phe Tyr Tyr Gly Gly Ala Ser  
 370 375 380  
 Ser Ala Ser Tyr Ala Ala  
 385 390

<210> 175  
 <211> 294  
 <212> PRT  
 <213> Homo sapiens

<400> 175  
 Met Asp Ser Glu Leu Met His Ser Ile Val Gly Ser Tyr His Lys Pro  
 1 5 10 15  
 Pro Glu Arg Val Phe Val Pro Ser Phe Thr Gln Asn Glu Pro Ser Gln  
 20 25 30  
 Asn Cys His Pro Ala Asn Leu Glu Val Thr Ser Pro Lys Ile Leu His  
 35 40 45  
 Ser Pro Asn Ser Gln Ala Leu Ile Leu Ala Leu Lys Thr Leu Gln Glu  
 50 55 60  
 Lys Ile His Arg Leu Glu Leu Glu Arg Thr Gln Ala Glu Asp Asn Leu  
 65 70 75 80  
 Asn Ile Leu Ser Arg Arg Ala Ala Gln Tyr Lys Lys Ala Leu Glu Asn  
 85 90 95  
 Glu Thr Asn Glu Arg Asn Leu Ala His Gln Glu Leu Ile Lys Gln Lys  
 100 105 110  
 Lys Asp Ile Ser Ile Gln Leu Ser Ser Ala Gln Ser Arg Cys Thr Leu  
 115 120 125  
 Leu Glu Lys Gln Leu Glu Tyr Thr Lys Arg Met Val Leu Asn Val Glu  
 130 135 140  
 Arg Glu Lys Asn Met Ile Leu Glu Gln Gln Ala Gln Leu Gln Arg Glu  
 145 150 155 160  
 Lys Glu Gln Asp Gln Met Lys Leu Tyr Ala Lys Leu Glu Lys Leu Asp  
 165 170 175  
 Val Leu Glu Lys Glu Cys Phe Arg Leu Thr Thr Thr Gln Lys Thr Ala  
 180 185 190  
 Glu Glu Lys Ile Lys His Leu Glu Glu Lys Leu Lys Glu Glu Glu His  
 195 200 205  
 Gln Arg Lys Leu Phe Gln Asp Lys Ala Ser Glu Lys Thr Lys Cys Ile  
 210 215 220  
 Lys Arg Arg Pro Pro Trp Gln Ile Cys Ser Lys Phe Gly Ala Leu Pro  
 225 230 235 240  
 Phe Val Ala Glu Lys Ser Thr Ser Ala Ser Cys Ser Val Asn Ala Ser  
 245 250 255  
 Met Gln Asn Phe Leu Gln Met Arg Gln His Arg Asp Pro His Ile Leu  
 260 265 270  
 Gln Lys Pro Phe Asn Val Thr Glu Thr Arg Cys Leu Pro Lys Pro Ser  
 275 280 285  
 Arg Thr Thr Ser Ser Val  
 290 294

<210> 176  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

<400> 176  
 Met Lys Ile Gly Ala Ile Thr Phe Gln Val Ala Thr Gly Asp Ile Ala  
 1 5 10 15  
 Thr Glu Gln Val Asp Val Ile Val Asn Ser Thr Ala Arg Thr Phe Asn  
 20 25 30  
 Arg Lys Ser Gly Val Ser Arg Ala Ile Leu Glu Gly Ala Gly Gln Ala  
 35 40 45  
 Val Glu Ser Glu Cys Ala Val Leu Ala Ala Gln Pro Leu Arg Arg Phe

50						55				60						
Tyr	Asn	Tyr	Thr	Arg	Trp	Met	Leu	Lys	Val	Gln	Asn	Asn	Asn	Ser	Cys	
65						70				75					80	
Ser	Trp	Gly	Lys	Arg	Cys	Gln	Glu	Asn	Gly	His	Gln	Cys	Ser	Arg	Arg	
				85					90					95	96	

<210> 177  
 <211> 128  
 <212> PRT  
 <213> Homo sapiens

<400> 177

Met	Lys	Arg	Cys	Gly	Arg	His	Gly	Glu	Ser	Thr	Asn	Leu	His	Lys	Thr	
1			5						10					15		
Ile	Lys	His	Ala	Glu	Met	Tyr	Lys	Leu	Thr	Gly	Leu	Lys	Ala	Ile	Met	
			20					25					30			
Pro	Ala	Arg	Arg	Ser	Gly	Gly	His	Phe	Ser	Gly	Trp	Thr	Gly	Ala	Ser	
		35					40					45				
His	Leu	Ser	Lys	Arg	Ile	Glu	Pro	Phe	Gln	Glu	Glu	Glu	Asn	Pro	Gln	
	50					55				60						
Arg	Gly	Val	Gln	Ile	Ala	Val	Ser	Ser	Ser	Gln	Lys	Ser	Gly	His	Asn	
65					70					75					80	
His	His	Pro	Asn	Arg	Asn	Val	Ala	Gln	Val	Gly	Arg	Lys	Lys	Gln	Tyr	
			85						90					95		
Thr	Ile	His	Leu	Gly	Pro	Asp	Glu	Lys	Leu	His	Glu	Ser	Pro	Ala	Gln	
			100				105						110			
Ser	Asn	Gln	Ala	Thr	Thr	Phe	Ser	Leu	Thr	Arg	Lys	Ser	Ser	Leu	Leu	
		115					120					125			128	

<210> 178  
 <211> 313  
 <212> PRT  
 <213> Homo sapiens

<400> 178

Met	Val	Lys	Ile	Lys	Glu	Glu	Pro	Met	Glu	Val	Asp	Ile	Gln	Asp	Ser	
1			5						10					15		
His	Val	Ser	Ile	Ser	Pro	Ser	Arg	Asn	Val	Gly	Tyr	Ser	Thr	Leu	Ile	
			20					25					30			
Gly	Arg	Glu	Lys	Thr	Glu	Pro	Leu	Gln	Lys	Met	Pro	Glu	Gly	Arg	Val	
		35					40					45				
Pro	Pro	Glu	Arg	Asn	Leu	Phe	Ser	Gln	Asp	Ile	Ser	Val	Lys	Met	Ala	
	50					55					60					
Ser	Glu	Leu	Leu	Phe	Gln	Leu	Ser	Glu	Lys	Val	Ser	Lys	Glu	His	Asn	
65				70					75						80	
His	Thr	Lys	Glu	Asn	Thr	Ile	Arg	Thr	Thr	Thr	Ser	Pro	Phe	Phe	Ser	
			85						90					95		
Glu	Asp	Thr	Phe	Arg	Gln	Ser	Pro	Phe	Thr	Ser	Asn	Ser	Lys	Glu	Leu	
		100					105						110			
Leu	Pro	Ser	Asp	Ser	Val	Leu	His	Gly	Arg	Ile	Ser	Ala	Pro	Glu	Thr	
		115					120					125				
Glu	Lys	Ile	Val	Leu	Glu	Ala	Gly	Asn	Gly	Leu	Pro	Ser	Trp	Lys	Phe	
	130					135					140					
Asn	Asp	Gln	Leu	Phe	Pro	Cys	Asp	Val	Cys	Gly	Lys	Val	Phe	Gly	Arg	
145					150					155					160	

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<210> 179
<211> 136
<212> PRT
<213> Homo sapiens
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<210> 180
<211> 302
<212> PRT
<213> Homo sapiens
```

136

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      50      55      60
Asn His Ser Asn Trp Ser Leu Glu Asp Thr Gly Ala Leu Leu Ser Ser
 65      70      75      80
Gly Gln Lys Asp Tyr Val Thr Val Gln Leu Gln Asn Gly Glu Ile Trp
      85      90      95
Glu Leu Ser Arg Cys Ser Arg Asn Lys Arg Glu Asn Thr Ser Ser Leu
      100      105      110
Gly Tyr Glu Tyr Thr Gly Ser Lys Lys Glu Phe Pro Cys Val Asp Gly
      115      120      125
Tyr Ile Tyr Asp Gln Asn Thr Trp Lys Ser Thr Ala Val Thr Gln Trp
      130      135      140
Asn Leu Val Cys Asp Arg Lys Trp Leu Ala Met Leu Ile Gln Pro Leu
      145      150      155      160
Phe Met Phe Gly Gly Pro Thr Gly Ile Gly Gly Leu Leu Ala Thr Phe
      165      170      175
Ser Asp Arg Leu Gly Arg Arg Val Val Leu Trp Ala Thr Ser Ser Ser
      180      185      190
Met Phe Leu Phe Gly Ile Ala Ala Phe Ala Val Asp Tyr Tyr Thr
      195      200      205
Phe Met Ala Ala Arg Phe Phe Ser Cys His Gly Cys Lys Trp Ile Ser
      210      215      220
Cys Gly Gly Val Cys Leu Cys Asp Gly Ile His Trp His Glu Val Ser
      225      230      235      240
Asp Met Gly Val Cys Pro Phe Ala Phe Leu Phe Cys Ser Trp Asn Pro
      245      250      255
Ala Gly Gly Phe Asp Arg Ile Leu Gly Gln Asp Leu Val Ala Leu Pro
      260      265      270
Asp Asp Pro Leu His Ser Asp Cys Pro Leu Tyr Pro Val Leu Leu Gly
      275      280      285
Ala Pro Arg Asp Thr Phe Leu Ala Ser Leu Arg Gly Thr Ile.
      290      295      300      302

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<210> 181  
 <211> 290  
 <212> PRT  
 <213> Homo sapiens

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      <400> 181
Met Leu Gln Arg Gly Ala Gln Pro Pro Met Val Ile Leu Arg Arg Ser
  1      5      10      15
Thr Asn Ala Gln Cys Ile Thr Val Asn Thr Lys Pro Ala Gln Leu Arg
      20      25      30
Pro Ala Ala Pro Ala Arg Leu Leu Arg Lys Asn Arg Leu His Pro Trp
      35      40      45
Ala Gly His Trp Leu His Val Arg Glu Asp Ile Cys Thr Glu Ala Met
      50      55      60
Leu Glu Asn Trp Ile Lys Leu Arg Tyr Ala Ser Gly Val Asn Asp Asn
      65      70      75      80
Leu Gln Lys Asn Leu Thr Leu Ser Lys Asn Leu Leu Asn Arg Glu Glu
      85      90      95
Asn Thr Leu Lys Asn Thr Gly Val Phe Ser Lys Pro Ser Ser Glu Cys
      100      105      110
Ser Met Lys Glu Gly Ile Gln Thr Cys Met Phe Pro Lys Glu Thr Asp
      115      120      125
Ile Lys Thr Ser Glu Asn Thr Ala Glu Phe Lys Glu Arg Glu Leu Cys
      130      135      140
Pro Leu Lys Thr Ser Lys Lys Leu Pro Glu Asn His Leu Pro Arg Asn
      145      150      155      160
Ser Pro Gln Tyr His Gln Pro Asp Leu Pro Glu Ile Ser Arg Lys Asn
      165      170      175
Asn Gly Asn Asn Gln Gln Val Pro Val Lys Asn Glu Val Asp His Cys

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      180      185      190
Glu Asn Leu Lys Lys Val Asp Thr Lys Pro Ser Ser Glu Lys Lys Ile
      195      200      205
His Lys Thr Ser Arg Glu Asp Met Phe Ser Glu Lys Gln Asp Ile Pro
      210      215      220
Phe Val Glu Gln Glu Asp Pro Tyr Arg Lys Lys Lys Leu Gln Glu Lys
      225      230      235      240
Arg Glu Gly Asn Leu Gln Asn Leu Asn Trp Ser Lys Ser Arg Thr Cys
      245      250      255
Arg Lys Asn Lys Lys Arg Gly Val Ala Pro Val Ser Arg Pro Pro Glu
      260      265      270
Gln Ser Asp Leu Lys Leu Val Cys Ser Asp Phe Glu Arg Ser Glu Leu
      275      280      285
Ser Ser
      290

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<210> 182
<211> 335
<212> PRT
<213> Homo sapiens

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      <400> 182
Met Ala Ser Asn Glu Arg Asp Ala Ile Ser Trp Tyr Gln Lys Lys Ile
  1      5      10      15
Gly Ala Tyr Asp Gln Gln Ile Trp Glu Lys Ser Ile Glu Gln Thr Gln
      20      25      30
Ile Lys Gly Leu Lys Asn Lys Pro Lys Lys Met Gly His Ile Lys Pro
      35      40      45
Asp Leu Ile Asp Val Asp Leu Ile Arg Gly Ser Thr Phe Ala Lys Ala
      50      55      60
Lys Pro Glu Ile Pro Trp Thr Ser Leu Thr Arg Lys Gly Leu Val Arg
      65      70      75      80
Val Val Phe Phe Pro Leu Phe Ser Asn Trp Trp Ile Gln Val Thr Ser
      85      90      95
Leu Arg Ile Phe Val Trp Leu Leu Leu Leu Tyr Phe Met Gln Val Ile
      100      105      110
Ala Ile Val Leu Tyr Leu Met Met Pro Ile Val Asn Ile Ser Glu Val
      115      120      125
Leu Gly Pro Leu Cys Leu Met Leu Leu Met Gly Thr Val His Cys Gln
      130      135      140
Ile Val Ser Thr Gln Ile Thr Arg Pro Ser Gly Asn Asn Gly Asn Arg
      145      150      155      160
Arg Arg Arg Lys Leu Arg Lys Thr Val Asn Gly Asp Gly Ser Arg Glu
      165      170      175
Asn Gly Asn Asn Ser Ser Asp Lys Val Arg Gly Ile Glu Thr Leu Glu
      180      185      190
Ser Val Pro Ile Ile Gly Gly Phe Trp Glu Thr Ile Phe Gly Asn Arg
      195      200      205
Ile Lys Arg Val Lys Leu Ile Ser Asn Lys Gly Thr Glu Thr Asp Asn
      210      215      220
Asp Pro Ser Cys Val His Pro Ile Ile Lys Arg Arg Gln Cys Arg Pro
      225      230      235      240
Glu Ile Arg Met Cys Gln Thr Arg Glu Lys Pro Lys Phe Ser Asp Gly
      245      250      255
Glu Lys Cys Arg Arg Glu Ala Phe Arg Arg Leu Gly Asn Gly Val Ser
      260      265      270
Asp Asp Leu Ser Ser Glu Glu Asp Gly Glu Ala Arg Thr Gln Met Ile
      275      280      285
Leu Leu Arg Arg Ser Val Glu Gly Ala Ser Ser Asp Asn Gly Cys Glu
      290      295      300
Val Lys Asn Arg Lys Ser Ile Leu Ser Arg His Leu Asn Ser Gln Val

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<210> 183
<211> 896
<212> PRT
<213> Homo sapiens
```

139



140

<210> 184  
 <211> 244  
 <212> PRT  
 <213> Homo sapiens

<400> 184  
 Met Ser Pro Val Phe Pro Met Leu Thr Val Leu Thr Met Phe Tyr Tyr  
 1 5 10 15  
 Ile Cys Leu Arg Arg Ala Arg Thr Ala Thr Arg Gly Glu Met Met  
 20 25 30  
 Asn Thr His Arg Ala Ile Glu Ser Asn Ser Gln Thr Ser Pro Leu Asn  
 35 40 45  
 Ala Glu Val Val Gln Tyr Ala Lys Glu Val Val Asp Phe Ser Ser His  
 50 55 60  
 Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met Trp Asn Leu Ala Gly  
 65 70 75 80  
 Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe Thr Gln Thr Ala Val  
 85 90 95  
 Phe Arg Thr Tyr Gly Thr Trp Trp Asp Gln Cys Pro Ser Ala Ser Leu  
 100 105 110  
 Pro Phe Lys Arg Thr Pro Pro Asn Phe Gln Ser Gln Asp Tyr Val Glu  
 115 120 125  
 Leu Thr Phe Glu Gln Gln Val Tyr Pro Thr Ala Val His Val Leu Glu  
 130 135 140  
 Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu Ala Cys Ser Ala Asn  
 145 150 155 160  
 Pro Tyr Ser Pro Asn Pro Pro Ala Glu Val Arg Trp Glu Ile Leu Trp  
 165 170 175  
 Ser Glu Arg Pro Thr Lys Val Asn Ala Ser Gln Ala Arg Gln Phe Lys  
 180 185 190  
 Pro Cys Ile Lys Gln Ile Asn Phe Pro Thr Asn Leu Ile Arg Leu Glu  
 195 200 205  
 Val Asn Ser Ser Leu Leu Glu Tyr Tyr Thr Glu Leu Asp Ala Val Val  
 210 215 220  
 Leu His Gly Val Lys Asp Lys Pro Val Leu Ser Leu Lys Thr Ser Leu  
 225 230 235 240  
 Ile Asp Met Glu  
 244

<210> 185  
 <211> 743  
 <212> PRT  
 <213> Homo sapiens

<400> 185  
 Met His Asn Leu Gln Thr Phe Leu Ala Asp Gly Asn Phe Leu Gln Thr  
 1 5 10 15  
 Leu Ala Ala Glu Val Glu Asn Met Lys Gln Leu Ile Tyr Leu Gly Leu  
 20 25 30  
 Ser Phe Tyr Glu Ile Thr Asp Ile Pro Glu Val Leu Glu Lys Leu Thr  
 35 40 45  
 Ala Val Asp Lys Leu Cys Met Ser Gly Asn Cys Val Glu Thr Leu Arg  
 50 55 60  
 Leu Gln Ala Leu Arg Lys Met Pro His Ile Lys His Val Asp Leu Arg  
 65 70 75 80  
 Leu Asn Val Ile Arg Lys Leu Ile Ala Asp Glu Val Asp Phe Leu Gln  
 85 90 95  
 His Val Thr Gln Leu Asp Leu Arg Asp Asn Lys Leu Gly Asp Leu Asp

142

Gly Tyr Thr Phe Leu His Pro Asn Val Val Pro Cys Pro His Gly Gln  
 610 615 620  
 Ser Gly Leu Leu Thr Pro Gln Glu Glu Phe Phe Ile Leu Gly Ser Lys  
 625 630 635 640  
 Gly Leu Trp Asp Arg Leu Ser Val Glu Glu Ala Ala Glu Ala Val Arg  
 645 650 655  
 Asn Val Pro Asp Ala Leu Ala Ala Lys Lys Leu Cys Thr Leu Ala  
 660 665 670  
 Gln Ser Tyr Gly Cys His Asp Ser Ile Ser Ala Val Val Val Gln Leu  
 675 680 685  
 Ser Val Thr Glu Asp Ser Phe Cys Cys Cys Glu Leu Ser Ala Gly Gly  
 690 695 700  
 Ala Val Pro Pro Pro Ser Pro Gly Ile Phe Pro Pro Ser Val Asn Met  
 705 710 715 720  
 Val Ile Lys Asp Arg Pro Ser Asp Gly Leu Gly Val Pro Ser Ser Ser  
 725 730 735  
 Ser Gly Met Ala Ser Arg Asp  
 740 743

<210> 186  
 <211> 131  
 <212> PRT  
 <213> Homo sapiens

<400> 186  
 Met Ala Ala Ile Leu Gly Asp Thr Ile Met Val Ala Lys Gly Leu Val  
 1 5 10 15  
 Lys Leu Thr Gln Ala Ala Val Glu Thr His Leu Gln His Leu Gly Ile  
 20 25 30  
 Gly Gly Glu Leu Ile Met Ala Ala Arg Ala Leu Gln Ser Thr Ala Val  
 35 40 45  
 Glu Gln Ile Gly Met Phe Leu Gly Lys Val Gln Gly Gln Asp Lys His  
 50 55 60  
 Glu Glu Tyr Phe Ala Arg Glu Leu Arg Arg Pro Arg Lys Gly Asp Pro  
 65 70 75 80  
 Leu Ile Ser Pro Ala Cys Arg Arg Ser Leu His Arg Leu Val Leu Ser  
 85 90 95  
 Leu Ser Ser Arg Pro Asp Ser Val Pro Ile Pro Gly Ala Cys Ala Gln  
 100 105 110  
 Arg Gly Pro Ser Ser Cys Pro Thr Trp Pro Val Asp Pro Leu Glu Lys  
 115 120 125  
 Pro Arg Pro  
 130 131

<210> 187  
 <211> 714  
 <212> PRT  
 <213> Homo sapiens

<400> 187  
 Met Lys Leu Lys Glu Leu Glu Arg Pro Ala Val Gln Ala Trp Ser Pro  
 1 5 10 15  
 Ala Ser Gln Tyr Pro Leu Tyr Leu Ala Thr Gly Thr Ser Ala Gln Gln  
 20 25 30  
 Leu Asp Ser Ser Phe Ser Thr Asn Gly Thr Leu Glu Ile Phe Glu Val  
 35 40 45  
 Asp Phe Arg Asp Pro Ser Leu Asp Leu Lys His Arg Gly Val Leu Ser  
 50 55 60  
 Ala Leu Ser Arg Phe His Lys Leu Val Trp Gly Ser Phe Gly Ser Gly

65					70					75				80	
Leu	Leu	Glu	Ser	Ser	Gly	Val	Ile	Val	Gly	Gly	Gly	Asp	Asn	Gly	Met
				85					90					95	
Leu	Ile	Leu	Tyr	Asn	Val	Thr	His	Ile	Leu	Ser	Ser	Gly	Lys	Glu	Pro
			100					105					110		
Val	Ile	Ala	Gln	Lys	Gln	Lys	His	Thr	Gly	Ala	Val	Arg	Ala	Leu	Asp
		115					120					125			
Leu	Asn	Pro	Phe	Gln	Gly	Asn	Leu	Leu	Ala	Ser	Gly	Ala	Ser	Asp	Ser
	130					135					140				
Glu	Ile	Phe	Ile	Trp	Asp	Leu	Asn	Asn	Leu	Asn	Val	Pro	Met	Thr	Leu
145					150				155					160	
Gly	Ser	Lys	Ser	Gln	Gln	Pro	Pro	Glu	Asp	Ile	Lys	Ala	Leu	Ser	Trp
			165					170						175	
Asn	Arg	Gln	Ala	Gln	His	Ile	Leu	Ser	Ser	Ala	His	Pro	Ser	Gly	Lys
		180					185					190			
Ala	Val	Val	Trp	Asp	Leu	Arg	Lys	Asn	Glu	Pro	Ile	Ile	Lys	Val	Ser
	195					200					205				
Asp	His	Ser	Asn	Arg	Met	His	Cys	Ser	Gly	Leu	Ala	Trp	His	Pro	Asp
210					215				220						
Ile	Ala	Thr	Gln	Leu	Val	Leu	Cys	Ser	Glu	Asp	Asp	Arg	Leu	Pro	Val
225				230					235					240	
Ile	Gln	Leu	Trp	Asp	Leu	Arg	Phe	Ala	Ser	Ser	Pro	Leu	Lys	Val	Leu
			245					250						255	
Glu	Ser	His	Ser	Arg	Gly	Ile	Leu	Ser	Val	Ser	Trp	Ser	Gln	Ala	Asp
		260				265						270			
Ala	Glu	Leu	Leu	Leu	Thr	Ser	Ala	Lys	Asp	Ser	Gln	Ile	Leu	Cys	Arg
	275					280					285				
Asn	Leu	Gly	Ser	Ser	Glu	Val	Val	Tyr	Lys	Leu	Pro	Thr	Gln	Ser	Ser
	290				295					300					
Trp	Cys	Phe	Asp	Val	Gln	Trp	Cys	Pro	Arg	Asp	Pro	Ser	Val	Phe	Ser
305				310					315					320	
Ala	Ala	Ser	Phe	Asn	Gly	Trp	Ile	Ser	Leu	Tyr	Ser	Val	Met	Gly	Arg
			325					330					335		
Ser	Trp	Glu	Val	Gln	His	Met	Arg	Gln	Ala	Asp	Lys	Ile	Ser	Ser	Ser
		340				345						350			
Phe	Ser	Lys	Gly	Gln	Pro	Leu	Pro	Pro	Leu	Gln	Val	Pro	Glu	Gln	Val
	355					360					365				
Ala	Gln	Ala	Pro	Leu	Ile	Pro	Pro	Leu	Lys	Lys	Pro	Pro	Lys	Trp	Ile
370					375						380				
Arg	Arg	Pro	Thr	Gly	Val	Ser	Phe	Ala	Phe	Gly	Gly	Lys	Leu	Val	Thr
385				390					395					400	
Phe	Gly	Leu	Pro	Ser	Thr	Pro	Ala	His	Leu	Val	Pro	Gln	Pro	Cys	Pro
			405					410					415		
Arg	Leu	Val	Phe	Ile	Ser	Gln	Val	Thr	Thr	Glu	Ser	Glu	Phe	Leu	Met
		420				425						430			
Arg	Ser	Ala	Glu	Leu	Gln	Glu	Ala	Leu	Gly	Ser	Gly	Asn	Leu	Leu	Asn
	435					440					445				
Tyr	Cys	Gln	Asn	Lys	Ser	Gln	Gln	Ala	Leu	Leu	Gln	Ser	Glu	Lys	Met
	450				455						460				
Leu	Trp	Gln	Phe	Leu	Lys	Val	Thr	Leu	Glu	Gln	Asp	Ser	Arg	Met	Lys
465				470					475					480	
Phe	Leu	Lys	Leu	Leu	Gly	Tyr	Ser	Lys	Asp	Glu	Leu	Gln	Lys	Lys	Val
			485					490					495		
Ala	Thr	Trp	Leu	Lys	Ser	Asp	Val	Gly	Leu	Gly	Glu	Ser	Pro	Gln	Pro
		500					505					510			
Lys	Gly	Asn	Asp	Leu	Asn	Ser	Asp	Arg	Gln	Gln	Ala	Phe	Cys	Ser	Gln
	515					520					525				
Ala	Ser	Lys	His	Thr	Thr	Lys	Glu	Ala	Ser	Ala	Ser	Ser	Ala	Phe	Phe
	530				535						540				
Asp	Glu	Leu	Val	Pro	Gln	Asn	Met	Thr	Pro	Trp	Glu	Ile	Pro	Ile	Thr
545				550					555					560	
Lys	Asp	Ile	Asp	Gly	Leu	Leu	Ser	Gln	Ala	Leu	Leu	Leu	Gly	Glu	Leu
			565					570					575		

Gly Pro Ala Val Glu Leu Cys Leu Lys Glu Glu Arg Phe Ala Asp Ala  
                   580                                  585                                  590  
 Ile Ile Leu Ala Gln Ala Gly Gly Thr Asp Leu Leu Lys Gln Thr Gln  
                   595                                  600                                  605  
 Glu Arg Tyr Leu Ala Lys Lys Lys Thr Lys Ile Ser Ser Leu Leu Ala  
                   610                                  615                                  620  
 Cys Val Val Gln Lys Asn Trp Lys Asp Val Val Cys Thr Cys Ser Leu  
                   625                                  630                                  635                                  640  
 Lys Asn Trp Arg Glu Ala Leu Ala Leu Leu Leu Thr Tyr Ser Gly Thr  
                                   645                                  650                                  655  
 Glu Lys Phe Pro Glu Leu Cys Asp Met Leu Gly Thr Arg Met Glu Gln  
                                   660                                  665                                  670  
 Glu Gly Ser Arg Ala Leu Thr Ser Glu Ala Arg Leu Cys Tyr Ala Ala  
                                   675                                  680                                  685  
 Leu Arg Gln Cys Thr Thr Ala Gly Val Val Leu Ala Gln Asn Ala Thr  
                                   690                                  695                                  700  
 Arg Leu Cys Pro Pro Trp Leu Cys Arg Thr  
                                   705                                  710                                  714

<210> 188  
 <211> 130  
 <212> PRT  
 <213> Homo sapiens

<400> 188  
 Met Thr Leu Val His His Gln Gly Asn Ser His Leu Ala Asn Gly Ile  
   1                                  5                                  10                                  15  
 Ala Gly Ser Met Ala Thr Leu Leu His Asp Ala Val Met Asn Pro Ala  
                                   20                                  25                                  30  
 Glu Val Val Lys Gln Arg Leu Gln Met Tyr Asn Ser Gln His Arg Ser  
                                   35                                  40                                  45  
 Ala Ile Ser Cys Ile Arg Thr Val Trp Arg Thr Asp Gly Leu Val Ala  
                                   50                                  55                                  60  
 Leu Leu Pro Glu Leu His His Pro Ala Asp His Glu His Pro Leu Pro  
                                   65                                  70                                  75                                  80  
 Val His Pro Leu Tyr His Leu Leu Val Pro Ala Gly Ala Gly Gln Pro  
                                   85                                  90                                  95  
 Pro Pro Asp Leu Gln Pro Ala Val Pro His His Leu Arg Arg Gly Gly  
                                   100                                  105                                  110  
 Arg Gly Pro Arg Arg Gly Arg His Asp Pro Pro Gly Arg Leu Val Arg  
                                   115                                  120                                  125  
 Pro Phe  
   130

<210> 189  
 <211> 129  
 <212> PRT  
 <213> Homo sapiens

<400> 189  
 Met Arg Arg Glu Gln Leu Pro Lys Ser Arg Gly Gly Glu Gly Cys Val  
   1                                  5                                  10                                  15  
 Gln Lys Ser Asp Leu Ser Arg Arg Tyr His Pro Gln Gly Arg Pro Asp  
                                   20                                  25                                  30  
 Arg Arg Ile Pro His Gly Asn Gln Gly Thr Thr Pro Pro Pro Thr Thr  
                                   35                                  40                                  45  
 Ser Leu Arg Pro Pro Ala Pro Ser Ser Pro Ala Pro Pro Leu Thr Gln  
                                   50                                  55                                  60  
 His Pro Lys Gly Gln Glu Thr Leu Met Thr Trp Pro Leu Gln Val Gln

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65          70          75          80
Pro Pro Gly Met Glu Gln Gly Arg Gly Met Gly Ser Gly Ser Gly Gly
          85          90          95
Val Ser Arg Glu Ser Phe Asn Pro Val Ile Val Arg Leu Ser Leu Arg
          100          105          110
Ser Arg Cys Ser Leu Phe Ser Ser Arg Leu Phe Arg Val Phe Arg Gly
          115          120          125
Asp
129

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<210> 190
<211> 56
<212> PRT
<213> Homo sapiens

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```

<400> 190
Met Arg Tyr Ser Thr Ser Ser Arg Glu Asn Lys Thr Gln Arg Asp Arg
1          5          10          15
Leu Lys Thr Asn Ser Val Asn Cys Tyr Val Gly Asn Tyr Ile Glu Tyr
          20          25          30
Leu Leu Ile Phe Gln Gly His Phe Ala Val Thr Glu Ser Glu Thr Glu
          35          40          45
Phe Val Lys Gln Met Lys Arg His
          50          55 56

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<210> 191
<211> 92
<212> PRT
<213> Homo sapiens

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```

<400> 191
Met Pro Ser Leu Ser Leu Cys Thr Leu His Pro Pro Glu Ile Met Pro
1          5          10          15
Leu Gly Tyr Gly Ala Ser Ser Phe Arg Thr Phe Pro Asn Pro Pro Gln
          20          25          30
Phe Ala Ala Thr Pro Phe Pro Pro Tyr Leu Phe Pro Ala Ser Ser Pro
          35          40          45
Gly Phe Pro Arg Gly Cys Gly Leu Ser Leu Ser Leu Leu Gly Tyr Thr
          50          55          60
Ser Leu Gly Ser Thr Ser Ser Gln Thr Glu Pro Arg Arg Cys Gln Ala
65          70          75          80
Glu Pro Ser Arg Gly Arg Gln Gly Ala Gly Arg Pro
          85          90          92

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<210> 192
<211> 48
<212> PRT
<213> Homo sapiens

```

```

<400> 192
Met Ile Leu Gln Cys Cys Asn Trp Val Val Leu Phe Lys Gln Ile Ile
1          5          10          15
Pro Ser Val Phe Lys Ala Phe Val Asn Lys Gly Phe Lys Met Phe Ser
          20          25          30
Tyr Ser Thr Gly Pro Glu Ile Pro Asn Phe Gly Ile Glu Asn Pro Glu
          35          40          45          48

```

<210> 193  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<400> 193  
 Met Ile Phe Lys Lys Tyr Asn Gln Val Leu Leu Ile Val Tyr Pro Ser  
 1 5 10 15  
 Gly Ile Ile Ser Thr Gln Ser Val Ile Ile Asp Leu Leu Pro Tyr Thr  
 20 25 30  
 Ile Thr Arg Ser Thr Asp Gly Val Phe Lys Ala Gln Arg Asn Ala Val  
 35 40 45  
 Thr Ser  
 50

<210> 194  
 <211> 266  
 <212> PRT  
 <213> Homo sapiens

<400> 194  
 Met Ser Arg Ile Ser His Trp His Ile Leu Ser Ile Asn Ser Asp Phe  
 1 5 10 15  
 Lys Leu Leu Asp His Leu Pro Val Asn Cys Tyr Glu Gln Leu Cys Ile  
 20 25 30  
 His Val Ser Leu Tyr Ser Leu Glu Ser Ser Arg Met Asp Arg Met Thr  
 35 40 45  
 Glu Asp Ala Leu Arg Leu Asn Leu Leu Lys Arg Ser Ser Asp Pro Ala  
 50 55 60  
 Asp Glu Arg Asp Asp Val Leu Ala Lys Arg Leu Lys Met Glu Gly His  
 65 70 75 80  
 Glu Ala Met Glu Arg Leu Lys Met Leu Ala Leu Leu Lys Arg Lys Asp  
 85 90 95  
 Leu Ala Asn Leu Gly Val Pro His Glu Leu Pro Thr Lys Gln Asp Gly  
 100 105 110  
 Arg Gly Gly Lys Gly Tyr Glu Glu Lys Leu Asn Gly Asn Leu Lys Pro  
 115 120 125  
 His Gly Asp Asn Arg Thr Ala Gly Arg Pro Gly Lys Glu Asn Ile Asn  
 130 135 140  
 Asp Glu Pro Val Asp Met Ser Ala Arg Arg Ser Glu Pro Glu Arg Gly  
 145 150 155 160  
 Arg Leu Thr Pro Ser Pro Asp Ile Ile Val Leu Ser Asp Asn Glu Ala  
 165 170 175  
 Ser Ser Pro Arg Ser Ser Ser Arg Met Glu Glu Arg Leu Lys Ala Ala  
 180 185 190  
 Asn Leu Glu Met Phe Lys Gly Lys Gly Ile Glu Glu Arg Gln Gln Leu  
 195 200 205  
 Ile Lys Gln Leu Arg Asp Glu Leu Arg Leu Glu Glu Ala Arg Leu Val  
 210 215 220  
 Leu Leu Lys Lys Leu Arg Gln Ser Gln Leu Gln Lys Glu Asn Val Val  
 225 230 235 240  
 Gln Lys Thr Pro Val Val Gln Asn Ala Ala Ser Ile Val Gln Pro Phe  
 245 250 255  
 Phe Phe Leu Cys Gly Thr Ala Gly Pro Ile  
 260 265 266



<210> 195  
 <211> 153  
 <212> PRT  
 <213> Homo sapiens

<400> 195  
 Met Cys Phe Asp Cys Phe Val Gly Gly Val Gly Lys Arg Val Glu Met  
 1 5 10 15  
 Lys Phe Leu Met Arg Lys Gly Val Gln Gln Ile Leu Gly Ser Val Gly  
 20 25 30  
 Ser Arg Ala Thr Val His Leu Gln Ile Pro Ser Arg Asp Leu Glu Thr  
 35 40 45  
 Gly Leu Pro Gly Thr Ile Leu Glu Thr Glu Asn Arg Ser Ala Ala Pro  
 50 55 60  
 Ile Thr Thr Thr Gly Thr Gln Ala Cys His Lys Gly Asp Leu Arg Ile  
 65 70 75 80  
 Asn Leu Pro Cys Pro Pro Gln Leu Ala Ser Ala Cys Thr Ile Arg Leu  
 85 90 95  
 Asn Leu Glu Glu Ile Glu Asn Leu Asn Arg Pro Ile Thr Gly Asn Glu  
 100 105 110  
 Ile Glu Ser Val Ile Ser Leu Pro Thr Lys Arg Ser Pro Val Val Asp  
 115 120 125  
 Asp Phe Ile Ala Glu Pro Tyr Gln Thr Tyr Arg Glu Lys Leu Thr Pro  
 130 135 140  
 Ile Leu His Lys Leu Phe Lys Asn Asn  
 145 150 153

<210> 196  
 <211> 63  
 <212> PRT  
 <213> Homo sapiens

<400> 196  
 Met Trp Lys Gly Gly Arg Ser His Pro Phe Leu Pro His Ser Ser Arg  
 1 5 10 15  
 Cys Ala Gly Ser Gly Gly Gln Leu Asp Ser Ile Leu Pro His Gln Ser  
 20 25 30  
 Pro Ala Trp Gly Pro Trp Gly Cys Lys Asp Leu Ser Ser Gly Phe Pro  
 35 40 45  
 Ser Phe Leu Thr Ser Ser Ile Leu Trp Lys Ser Ala Val Val Lys  
 50 55 60 63

<210> 197  
 <211> 908  
 <212> PRT  
 <213> Homo sapiens

<400> 197  
 Met Ser Gly Gly Gly Gly Gly Gly Gly Ser Ala Pro Ser Arg Phe Ala  
 1 5 10 15  
 Asp Tyr Phe Val Ile Cys Gly Leu Asp Thr Glu Thr Gly Leu Glu Pro  
 20 25 30  
 Asp Glu Leu Ser Ala Leu Cys Gln Tyr Ile Gln Ala Ser Lys Ala Arg  
 35 40 45  
 Asp Gly Ala Ser Pro Phe Ile Ser Ser Thr Thr Glu Gly Glu Asn Phe  
 50 55 60  
 Glu Gln Thr Pro Leu Arg Arg Thr Phe Lys Ser Lys Val Leu Ala Arg  
 65 70 75 80

Tyr Pro Glu Asn Val Glu Trp Asn Pro Phe Asp Gln Asp Ala Val Gly  
                                   85                                  90                                  95  
 Met Leu Cys Met Pro Lys Gly Leu Ala Phe Lys Thr Gln Ala Asp Pro  
                                   100                                  105                                  110  
 Arg Glu Pro Gln Phe His Ala Phe Ile Ile Thr Arg Glu Asp Gly Ser  
                                   115                                  120                                  125  
 Arg Thr Phe Gly Phe Ala Leu Thr Phe Tyr Glu Glu Val Thr Ser Lys  
                                   130                                  135                                  140  
 Gln Ile Cys Ser Ala Met Gln Thr Leu Tyr His Met His Asn Ala Glu  
 145                                  150                                  155                                  160  
 Tyr Asp Val Leu His Ala Pro Pro Ala Asp Asp Arg Asp Gln Ser Ser  
                                   165                                  170                                  175  
 Met Glu Asp Gly Glu Asp Thr Pro Val Thr Lys Leu Gln Arg Phe Asn  
                                   180                                  185                                  190  
 Ser Tyr Asp Ile Ser Arg Asp Thr Leu Tyr Val Ser Lys Cys Ile Cys  
                                   195                                  200                                  205  
 Leu Ile Thr Pro Met Ser Phe Met Lys Ala Cys Arg Ser Val Leu Gln  
                                   210                                  215                                  220  
 Gln Leu His Gln Ala Val Thr Ser Pro Gln Pro Pro Pro Leu Pro Leu  
 225                                  230                                  235                                  240  
 Glu Ser Tyr Ile Tyr Asn Val Leu Tyr Glu Val Pro Leu Pro Pro Pro  
                                   245                                  250                                  255  
 Gly Arg Ser Leu Lys Phe Ser Gly Val Tyr Gly Pro Ile Ile Cys Gln  
                                   260                                  265                                  270  
 Arg Pro Ser Thr Asn Glu Leu Pro Leu Phe Asp Phe Pro Val Lys Glu  
                                   275                                  280                                  285  
 Val Phe Glu Leu Leu Gly Val Glu Asn Val Phe Gln Leu Phe Thr Cys  
                                   290                                  295                                  300  
 Ala Leu Leu Glu Phe Gln Ile Leu Leu Tyr Ser Gln His Tyr Gln Arg  
 305                                  310                                  315                                  320  
 Leu Met Thr Val Ala Glu Thr Ile Thr Ala Leu Met Phe Pro Phe Gln  
                                   325                                  330                                  335  
 Trp Gln His Val Tyr Val Pro Ile Leu Pro Ala Ser Leu Leu His Phe  
                                   340                                  345                                  350  
 Leu Asp Ala Pro Val Pro Tyr Leu Met Gly Leu His Ser Asn Gly Leu  
                                   355                                  360                                  365  
 Asp Asp Arg Ser Lys Leu Glu Leu Pro Gln Glu Ala Asn Leu Cys Phe  
                                   370                                  375                                  380  
 Val Asp Ile Asp Asn His Phe Ile Glu Leu Pro Glu Asp Leu Pro Gln  
 385                                  390                                  395                                  400  
 Phe Pro Asn Lys Leu Glu Phe Val Gln Glu Val Ser Glu Ile Leu Met  
                                   405                                  410                                  415  
 Ala Phe Gly Ile Pro Pro Glu Gly Asn Leu His Cys Ser Glu Ser Ala  
                                   420                                  425                                  430  
 Ser Lys Leu Lys Arg Leu Arg Ala Ser Glu Leu Val Ser Asp Lys Arg  
                                   435                                  440                                  445  
 Asn Gly Asn Ile Ala Gly Ser Pro Leu His Ser Tyr Glu Leu Leu Lys  
                                   450                                  455                                  460  
 Glu Asn Glu Thr Ile Ala Arg Leu Gln Ala Leu Val Lys Arg Thr Gly  
 465                                  470                                  475                                  480  
 Val Ser Leu Glu Lys Leu Glu Val Arg Glu Asp Pro Ser Ser Asn Lys  
                                   485                                  490                                  495  
 Asp Leu Lys Val Gln Cys Asp Glu Glu Glu Leu Arg Ile Tyr Gln Leu  
                                   500                                  505                                  510  
 Asn Ile Gln Ile Arg Glu Val Phe Ala Asn Arg Phe Thr Gln Met Phe  
                                   515                                  520                                  525  
 Ala Asp Tyr Glu Val Phe Val Ile Gln Pro Ser Gln Asp Lys Glu Ser  
                                   530                                  535                                  540  
 Trp Phe Thr Asn Arg Glu Gln Met Gln Asn Phe Asp Lys Ala Ser Phe  
 545                                  550                                  555                                  560  
 Leu Ser Asp Gln Pro Glu Pro Tyr Leu Pro Phe Leu Ser Arg Phe Leu  
                                   565                                  570                                  575  
 Glu Thr Gln Met Phe Ala Ser Phe Ile Asp Asn Lys Ile Met Cys His

```

      580      585      590
Asp Asp Asp Asp Lys Asp Pro Val Leu Arg Val Phe Asp Ser Arg Val
      595      600      605
Asp Lys Ile Arg Leu Leu Asn Val Arg Thr Pro Thr Leu Arg Thr Ser
      610      615      620
Met Tyr Gln Lys Cys Thr Thr Val Asp Glu Ala Glu Lys Ala Ile Glu
      625      630      635      640
Leu Arg Leu Ala Lys Ile Asp His Thr Ala Ile His Pro His Leu Leu
      645      650      655
Asp Met Lys Ile Gly Gln Gly Lys Tyr Glu Pro Gly Phe Phe Pro Lys
      660      665      670
Leu Gln Ser Asp Val Leu Ser Thr Gly Pro Ala Ser Asn Lys Trp Thr
      675      680      685
Lys Arg Asn Ala Pro Ala Gln Trp Arg Arg Lys Asp Arg Gln Lys Gln
      690      695      700
His Thr Glu His Leu Arg Leu Asp Asn Asp Gln Arg Glu Lys Tyr Ile
      705      710      715      720
Gln Glu Ala Arg Thr Met Gly Ser Thr Ile Arg Gln Pro Lys Leu Ser
      725      730      735
Asn Leu Ser Pro Ser Val Ile Ala Gln Thr Asn Trp Lys Phe Val Glu
      740      745      750
Gly Leu Leu Lys Glu Cys Arg Asn Lys Thr Lys Arg Met Leu Val Glu
      755      760      765
Lys Met Gly Arg Glu Ala Val Glu Leu Gly His Gly Glu Val Asn Ile
      770      775      780
Thr Gly Val Glu Glu Asn Thr Leu Ile Ala Ser Leu Cys Asp Leu Leu
      785      790      795      800
Glu Arg Ile Trp Ser His Gly Leu Gln Val Lys Gln Gly Lys Ser Ala
      805      810      815
Leu Trp Ser His Leu Leu His Tyr Gln Asp Asn Arg Gln Arg Lys Leu
      820      825      830
Thr Ser Gly Ser Leu Ser Thr Ser Gly Ile Leu Leu Asp Ser Glu Arg
      835      840      845
Arg Lys Ser Asp Ala Ser Ser Leu Met Pro Pro Leu Arg Ile Ser Leu
      850      855      860
Ile Gln Asp Met Arg His Ile Gln Asn Ile Gly Glu Ile Lys Thr Asp
      865      870      875      880
Val Gly Lys Ala Arg Ala Trp Val Arg Leu Ser Met Glu Lys Lys Leu
      885      890      895
Leu Ser Arg His Leu Lys Gln Arg Thr Ile Thr Pro
      900      905      908

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<210> 198  
 <211> 142  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 198
Met Leu Met Ser Glu Ala Leu Trp Asn Ile Gly Asp Ile Glu Leu Asp
  1      5      10      15
Ser Ser Leu Arg Gly His Leu Ser Ser Leu Ala Phe His Leu Thr Gly
      20      25      30
Glu Val Gly Ala Met Val Leu Gly Pro Gly Gly Glu Gly Glu Leu Arg
      35      40      45
Gly Ala Gly Gly Leu Gly Val Gln Gly Ala Glu Gly Ile Pro Arg Pro
      50      55      60
Gly Glu Cys Glu Arg Trp Ser Arg Phe Thr Gly Ser Trp Lys Ala Ala
      65      70      75      80
Ala Gln Pro Cys Gly Ala Ala Gly Leu Gln Arg Leu Gln Lys Val Asp
      85      90      95
Val Gly Phe Leu Tyr Gln Gly Cys His Leu Gln Val Gln Leu Ile Leu

```

```

      100      105      110
Leu Val Ala Ile Phe Tyr Ile Pro Ser Ser Leu His Ala Glu Glu Ile
      115      120      125
Ala Ser Arg Arg Asn Arg Arg Pro Gly Lys Ser Leu Val Ala
      130      135      140      142

```

<210> 199  
 <211> 46  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 199
Met Ile Ser Asp Leu Ser Gln Ile Ile Glu Ala Leu Gln Lys Ala Glu
  1           5           10           15
Ala Cys Ser Met Tyr Gln Leu Ser Glu Ile Ser Glu Lys Asp Leu Cys
      20           25           30
Val Ser Leu Thr Glu Asn Asp Ala Pro Leu Thr Leu Arg Ser
      35           40           45  46

```

<210> 200  
 <211> 55  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 200
Met Ala Gly Val Phe Trp Asp Ala Gln Gly Asn Met Pro Ala Asp Phe
  1           5           10           15
Leu Glu Gly Gln Arg Thr Ile Thr Ser Ala Tyr Tyr Glu Met Thr Trp
      20           25           30
Arg Lys Leu Ala Lys Asp Phe Ser Arg Lys Thr Pro Arg Lys Ala Ser
      35           40           45
Pro Lys Ser Pro Ser Lys Pro
      50           55

```

<210> 201  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 201
Met Lys Leu Ala Leu Glu Thr Thr Leu Cys Ala Leu Phe Leu Arg Leu
  1           5           10           15
Gln Gln Leu Leu His Gln Arg Thr His Pro Val Phe Ile Thr His Ile
      20           25           30
Arg Ala His Ser Ser Leu Pro Gly Pro Leu Ala Tyr Gly Asn Asp Gln
      35           40           45
Ala Ala Leu Gln Val Val Thr Ser Leu Leu Asp Gln Ala Thr Gln Leu
      50           55           60
His Gln Phe Phe Tyr Tyr Asn
      65           70  71

```

<210> 202  
 <211> 104  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 202

```

Met Gln Asp Pro Leu Glu Met Arg Trp Arg Glu Thr Phe Ser Thr His
 1           5           10           15
Gln Ser Glu Ala Val Tyr Ser Thr Arg Cys Ile Pro Asp Glu Glu Gly
           20           25           30
Pro Val Cys Cys Ala Ala Asn Ser Gly Phe Ser Ser Val Gln Val Tyr
           35           40           45
Ala His Ala Thr Thr Phe Val His Gln His Phe Cys Phe Gly Leu Phe
           50           55           60
Ser Asp Val Asn Glu Gln Glu Ala Lys Ile Leu Met Glu Thr Ile Asn
           65           70           75           80
Asn Leu Lys Lys Ile His Ile Gln Asn Gly Ile Lys Ala Ala Gln His
           85           90           95
Asp Lys Ser Ile Tyr Ala Ile Pro
           100           104

```

&lt;210&gt; 203

&lt;211&gt; 200

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

```

Met Asp Arg Asn Leu Gly Pro Thr Asp Gly Asn Pro Gly Arg Asp Arg
 1           5           10           15
Arg Leu Pro Ala Ser Gly Ser Ser Ser Ser Leu Ser Ala Ala Ser Ala
           20           25           30
Gly Leu Pro Gln Ala Leu His Arg Arg Arg Gln Ala Ser Gly Ala Ala
           35           40           45
Pro Gly Ser Trp Val Thr Gly Ser Arg Leu Pro Pro Asp Cys Gly Leu
           50           55           60
Leu Arg Arg Leu Ser Val Leu Leu Ser Leu Gly Leu Ala Leu Ser Gly
           65           70           75           80
Ser Thr Gly Glu Gly Arg Val Arg Arg Leu Arg Gly Arg Cys Arg Thr
           85           90           95
Lys Pro Tyr Ser Arg Cys Trp Thr Gly Thr Gly Ser Cys Gly Gly Asp
           100           105           110
Arg Glu Pro Pro Thr Leu Ala Leu Ala Leu Pro Ala Pro Ala Leu Glu
           115           120           125
Ala Leu Val Tyr Leu Thr Ile Val Glu Phe Ile Glu Asp Val Ser Ala
           130           135           140
Arg Thr Gly Val Gln Leu Pro Ile Leu Gly Gly Pro Gln Ser Val Lys
           145           150           155           160
Leu Phe Val Lys Ser Gly Ala Pro Pro Ser Ala Val Glu Ile Leu Val
           165           170           175
Arg Gly Ser Tyr His Glu Phe Leu Glu Thr Leu Asp Pro His Phe Pro
           180           185           190
Arg Ala Lys Ser Tyr Phe Leu Ala
           195           200

```

&lt;210&gt; 204

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

```

Met Val Val Gly Met Asp Ile Pro His Leu His Val Ile Asn Leu Pro
 1           5           10           15
Lys Pro Val Phe Ser Tyr Ile Lys Tyr Arg Leu Gln Lys Tyr Leu Leu

```

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<210> 205
<211> 140
<212> PRT
<213> Homo sapiens
```

```
<210> 206
<211> 45
<212> PRT
<213> Homo sapiens
```

```
<210> 207
<211> 219
<212> PRT
<213> Homo sapiens
```

153

```

65          70          75          80
Met Lys Asn Leu Val Leu Lys Leu Arg Ala Ser Ser His Asn Leu Gln
      85          90          95
Asn Tyr Ile Ser Ser Arg Arg Arg Ser Pro Ala Tyr Asp Gly Asn Thr
      100        105        110
Ser Arg Lys Ala Pro Asn Glu Phe Leu Thr Ser Val Val Glu Leu Ile
      115        120        125
Gly Ala Ala Lys Ala Leu Leu Ala Trp Leu Asp Arg Ala Pro Phe Thr
      130        135        140
Gly Ile Thr Asp Phe Ser Val Thr Lys Asn Lys Ile Ile Gln Leu Cys
145          150        155        160
Leu Asp Leu Thr Thr Thr Val Gln Lys Asp Cys Phe Val Ala Glu Met
      165        170        175
Glu Asp Lys Val Leu Thr Val Val Lys Val Leu Asn Gly Ile Cys Asp
      180        185        190
Lys Thr Ile Arg Ser Thr Thr Asp Pro Val Met Ser Gln Trp Ala Leu
      195        200        205
Pro Gly Gly Ser Ser Leu Thr Lys His Tyr Asp
210          215        219

```

<210> 208  
 <211> 167  
 <212> PRT  
 <213> Homo sapiens

```

<400> 208
Met Thr Gly Ala Leu Pro Pro Ser Ala Thr Thr Trp Arg Phe Arg Tyr
 1          5          10          15
Ser Glu Asp Arg Pro Phe Ile Trp Asp Cys Cys Asp Tyr Ser Cys Lys
      20        25        30
Asn Leu Ile Asp Leu Gln Lys His Leu Asp Thr His Ser Glu Glu Pro
      35        40        45
Ala Tyr Arg Cys Asp Phe Glu Asn Cys Thr Phe Ser Ala Arg Ser Leu
      50        55        60
Cys Ser Ile Lys Ser His Tyr Arg Lys Val His Glu Gly Asp Ser Glu
      65        70        75        80
Pro Arg Tyr Lys Cys His Val Cys Asp Lys Cys Phe Thr Arg Gly Asn
      85        90        95
Asn Leu Thr Val His Leu Arg Lys Lys His Gln Phe Lys Trp Pro Ser
      100       105       110
Gly His Pro Arg Phe Arg Tyr Lys Glu His Glu Asp Gly Tyr Met Arg
      115       120       125
Leu Gln Leu Val Arg Tyr Glu Ser Val Glu Leu Thr Gln Gln Leu Leu
      130       135       140
Arg Gln Pro Gln Glu Gly Ser Gly Leu Gly Thr Ser Leu His Thr Arg
145          150        155        160
Ala Ala Ser Arg Ala Leu Phe
      165        167

```

<210> 209  
 <211> 192  
 <212> PRT  
 <213> Homo sapiens

```

<400> 209
Met Val Gly Gln Val His Gly Gly Leu Met Gly Val Ile Gln Arg Ala
 1          5          10          15
Met Val Lys Ala Cys Pro His Val Trp Phe Glu Arg Ser Glu Val Lys
      20        25        30

```

```

Asp Arg His Leu Val Ala Lys Arg Leu Thr Glu His Val Gln Asp Lys
      35              40              45
Ser Lys Leu Pro Ile Leu Ile Phe Pro Glu Gly Thr Cys Ile Asn Asn
      50              55              60
Thr Ser Val Met Met Phe Lys Lys Gly Ser Phe Glu Ile Gly Ala Thr
      65              70              75              80
Val Tyr Pro Val Ala Ile Lys Tyr Asp Pro Gln Phe Gly Asp Ala Phe
              85              90              95
Trp Asn Ser Ser Lys Tyr Gly Met Val Thr Tyr Leu Leu Arg Met Met
              100             105             110
Thr Ser Trp Ala Ile Val Cys Ser Val Trp Tyr Leu Pro Pro Met Thr
              115             120             125
Arg Glu Ala Asp Glu Asp Ala Val Gln Phe Ala Asn Arg Val Lys Ser
              130             135             140
Ala Ile Ala Arg Gln Gly Gly Leu Val Asp Leu Leu Trp Asp Gly Gly
      145              150              155              160
Leu Lys Arg Glu Lys Val Lys Asp Thr Phe Lys Glu Glu Gln Gln Lys
              165              170              175
Leu Tyr Ser Lys Met Ile Val Gly Asn His Lys Asp Arg Ser Arg Ser
              180             185             190             192

```

<210> 210  
 <211> 590  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 210
Met Cys Ser Met Pro Arg Ser Leu Trp Leu Gly Cys Ser Ser Leu Ala
  1              5              10              15
Asp Ser Met Pro Ser Leu Arg Cys Leu Tyr Asn Pro Gly Thr Gly Ala
      20              25              30
Leu Thr Ala Phe Gln Asn Ser Ser Glu Arg Glu Asp Cys Asn Asn Gly
      35              40              45
Glu Pro Pro Arg Lys Ile Ile Pro Glu Lys Asn Ser Leu Arg Gln Thr
      50              55              60
Tyr Asn Ser Cys Ala Arg Leu Cys Leu Asn Gln Glu Thr Val Cys Leu
      65              70              75              80
Ala Ser Thr Ala Met Lys Thr Glu Asn Cys Val Ala Lys Thr Lys Leu
              85              90              95
Ala Asn Gly Thr Ser Ser Met Ile Val Pro Lys Gln Arg Lys Leu Ser
              100             105             110
Ala Ser Tyr Glu Lys Glu Lys Glu Leu Cys Val Lys Tyr Phe Glu Gln
              115             120             125
Trp Ser Glu Ser Asp Gln Val Glu Phe Val Glu His Leu Ile Ser Gln
      130             135             140
Met Cys His Tyr Gln His Gly His Ile Asn Ser Tyr Leu Lys Pro Met
      145             150             155             160
Leu Gln Arg Asp Phe Ile Thr Ala Leu Pro Ala Arg Gly Leu Asp His
              165              170              175
Ile Ala Glu Asn Ile Leu Ser Tyr Leu Asp Ala Lys Ser Leu Cys Ala
              180             185             190
Ala Glu Leu Val Cys Lys Glu Trp Tyr Arg Val Thr Ser Asp Gly Met
      195             200             205
Leu Trp Lys Lys Leu Ile Glu Arg Met Val Arg Thr Asp Ser Leu Trp
      210             215             220
Arg Gly Leu Ala Glu Arg Arg Gly Trp Gly Gln Tyr Leu Phe Lys Asn
      225             230             235             240
Lys Pro Pro Asp Gly Asn Ala Pro Pro Asn Ser Phe Tyr Arg Ala Leu
              245             250             255

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Tyr Pro Lys Ile Ile Gln Asp Ile Glu Thr Ile Glu Ser Asn Trp Arg  
 260 265 270  
 Cys Gly Arg His Ser Leu Gln Arg Ile His Cys Arg Ser Glu Thr Ser  
 275 280 285  
 Lys Gly Val Tyr Cys Leu Gln Tyr Asp Asp Gln Lys Ile Val Ser Gly  
 290 295 300  
 Leu Arg Asp Asn Thr Ile Lys Ile Trp Asp Lys Asn Thr Leu Glu Cys  
 305 310 315 320  
 Lys Arg Ile Leu Thr Gly His Thr Gly Ser Val Leu Cys Leu Gln Tyr  
 325 330 335  
 Asp Glu Arg Val Ile Ile Thr Gly Ser Ser Asp Ser Thr Val Arg Val  
 340 345 350  
 Trp Asp Val Asn Thr Gly Glu Met Leu Asn Thr Leu Ile His His Cys  
 355 360 365  
 Glu Ala Val Leu His Leu Arg Phe Asn Asn Gly Met Met Val Thr Cys  
 370 375 380  
 Ser Lys Asp Arg Ser Ile Ala Val Trp Asp Met Ala Ser Pro Thr Asp  
 385 390 395 400  
 Ile Thr Leu Arg Arg Val Leu Val Gly His Arg Ala Ala Val Asn Val  
 405 410 415  
 Val Asp Phe Asp Asp Lys Tyr Ile Val Ser Ala Ser Gly Asp Arg Thr  
 420 425 430  
 Ile Lys Val Trp Asn Thr Ser Thr Cys Glu Phe Val Arg Thr Leu Asn  
 435 440 445  
 Gly His Lys Arg Gly Ile Ala Cys Leu Gln Tyr Arg Asp Arg Leu Val  
 450 455 460  
 Val Ser Gly Ser Ser Asp Asn Thr Ile Arg Leu Trp Asp Ile Glu Cys  
 465 470 475 480  
 Gly Ala Cys Leu Arg Val Leu Glu Gly His Glu Glu Leu Val Arg Cys  
 485 490 495  
 Ile Arg Phe Asp Asn Lys Arg Ile Val Ser Gly Ala Tyr Asp Gly Lys  
 500 505 510  
 Ile Lys Val Trp Asp Leu Val Ala Ala Leu Asp Pro Arg Ala Pro Ala  
 515 520 525  
 Gly Thr Leu Cys Leu Arg Thr Leu Val Glu His Ser Gly Arg Val Phe  
 530 535 540  
 Arg Leu Gln Phe Asp Glu Phe Gln Ile Val Ser Ser Ser His Asp Asp  
 545 550 555 560  
 Thr Ile Leu Ile Trp Asp Phe Leu Asn Asp Pro Ala Ala Gln Ala Glu  
 565 570 575  
 Pro Pro Arg Ser Pro Ser Arg Thr Tyr Thr Tyr Ile Ser Arg  
 580 585 590

<210> 211  
 <211> 84  
 <212> PRT  
 <213> Homo sapiens

<400> 211  
 Met Ser Ser Ser Cys Asp Leu Pro Ser Leu Cys Glu Ser Asp Ser Thr  
 1 5 10 15  
 Arg Pro His Ala Phe Phe Leu Ala Gly Val Pro Asn Phe Pro Ser Tyr  
 20 25 30  
 Phe Cys Ile Ile Ser Val Ser His Arg Phe Pro Val Pro Lys Ile Pro  
 35 40 45  
 Pro Cys Pro Gln Ala Leu Arg Val Trp Asp Ile Ser Arg Asp Glu Glu  
 50 55 60  
 Arg Val Leu Ser Phe Leu Leu Leu Ser Pro Glu Leu Arg Ala Val Phe  
 65 70 75 80  
 Thr Phe Pro Gly  
 84

<210> 212  
 <211> 320  
 <212> PRT  
 <213> Homo sapiens

<400> 212  
 Met Pro Gln Asn Ala Val His Thr Met Tyr Cys Cys Pro Gln Asn Leu  
 1 5 10 15  
 Leu Leu Val Leu Glu Gly Lys Asp His Arg Ala Phe Ser Ala Val Ser  
 20 25 30  
 Pro Cys Val Thr Gly Ser Gly Gly Arg Ala Leu Arg Gly Ala Val Ala  
 35 40 45  
 Pro Arg Trp Gln Asn Ser Ala Ser Glu Ser His Ala Ala Glu Arg Asp  
 50 55 60  
 Gly Trp Glu Lys Ala Glu Cys Val Lys Lys Gly Val Lys Gly Pro Lys  
 65 70 75 80  
 Phe Ala Val Cys Gln Glu Tyr Lys Gly Cys Ser Gly Ile Arg Ala Glu  
 85 90 95  
 Cys Thr Leu Gln Ile Lys Met Asn Ala Met Leu Glu Thr Pro Glu Leu  
 100 105 110  
 Pro Ala Val Phe Asp Gly Val Lys Leu Ala Ala Val Ala Val Leu  
 115 120 125  
 Tyr Val Ile Val Arg Cys Leu Asn Leu Lys Ser Pro Thr Ala Pro Pro  
 130 135 140  
 Asp Leu Tyr Phe Gln Asp Ser Gly Leu Ser Arg Phe Leu Leu Lys Ser  
 145 150 155 160  
 Cys Pro Leu Leu Thr Lys Glu Tyr Ile Pro Pro Leu Ile Trp Gly Lys  
 165 170 175  
 Ser Gly His Ile Gln Thr Ala Leu Tyr Gly Lys Met Gly Arg Val Arg  
 180 185 190  
 Ser Pro His Pro Tyr Gly His Arg Lys Phe Ile Thr Met Ser Asp Gly  
 195 200 205  
 Ala Thr Ser Thr Phe Asp Leu Phe Glu Pro Leu Ala Glu His Cys Val  
 210 215 220  
 Gly Asp Asp Ile Thr Met Val Ile Cys Pro Gly Ile Ala Asn His Ser  
 225 230 235 240  
 Glu Lys Gln Tyr Ile Arg Thr Phe Val Asp Tyr Ala Gln Lys Asn Gly  
 245 250 255  
 Tyr Arg Cys Ser Arg Ala Glu Pro Ser Ala Val Pro Met Pro Asn Ile  
 260 265 270  
 Glu Leu Thr Ser Pro Arg Met Phe Thr Tyr Gly Cys Thr Trp Asp Phe  
 275 280 285  
 Gly Ala Ile Val Asn Tyr Ile Lys Lys Thr Tyr Ser Leu Thr Gln Leu  
 290 295 300  
 Val Val Val Gly Phe Ser Leu Gly Gly Asn Ile Val Cys Lys Tyr Leu  
 305 310 315 320

<210> 213  
 <211> 140  
 <212> PRT  
 <213> Homo sapiens

<400> 213  
 Met Gln Arg Leu Leu Leu Leu Pro Phe Leu Leu Leu Gly Thr Val Ser  
 1 5 10 15  
 Ala Leu His Leu Glu Asn Asp Ala Pro His Leu Glu Ser Leu Glu Thr

```

      20      25      30
Gln Ala Asp Leu Gly Gln Asp Leu Asp Ser Ser Lys Glu Gln Glu Arg
      35      40      45
Asp Leu Ala Leu Thr Glu Glu Val Ile Gln Ala Glu Gly Glu Glu Val
      50      55      60
Lys Ala Ser Ala Cys Gln Asp Asn Phe Glu Asp Glu Glu Ala Met Glu
      65      70      75      80
Ser Asp Pro Ala Ala Leu Asp Lys Asp Phe Gln Cys Pro Arg Glu Glu
      85      90      95
Asp Ile Val Glu Val Gln Gly Ser Pro Arg Cys Lys Thr Cys Arg Tyr
      100      105      110
Leu Leu Val Arg Thr Pro Lys Thr Phe Ala Glu Ala Gln Asn Val Cys
      115      120      125
Ser Arg Cys Tyr Gly Gly Asn Leu Gly Leu Tyr Ser
      130      135      140

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<210> 214  
 <211> 38  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 214
Met Val Glu Leu Leu Ser Glu Glu Glu Ile Ile Pro Val Leu Ser Asn
  1      5      10      15
Ser Pro Arg Lys Leu Lys Lys Arg Glu Cys Pro Val Thr Gln Ser Thr
      20      25      30
Arg Pro Ala Phe Pro Cys
      35      38

```

<210> 215  
 <211> 377  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 215
Met Ala Val Pro Gly Ser Glu Phe Glu Gly His Lys Arg Ile Ser Glu
  1      5      10      15
Gln Pro Leu Pro Asn Lys Thr Ile Ser Pro Pro Pro Ala Pro Ala Pro
      20      25      30
Ala Ala Ala Pro Leu Pro Cys Gly Pro Thr Glu Thr Ile Pro Ser Phe
      35      40      45
Leu Leu Thr Arg Ala Gly Arg Asp Gln Ala Ile Cys Glu Leu Gln Glu
      50      55      60
Glu Val Ser Arg Leu Arg Leu Arg Leu Glu Asp Ser Leu His Arg Pro
      65      70      75      80
Leu Gln Gly Ser Pro Thr Arg Pro Ala Ser Ala Phe Asp Arg Pro Ala
      85      90      95
Arg Thr Arg Gly Arg Pro Ala Asp Ser Pro Ala Thr Trp Gly Ser His
      100      105      110
Tyr Gly Ser Lys Ser Thr Glu Arg Leu Pro Gly Glu Pro Arg Gly Glu
      115      120      125
Glu Gln Ile Val Pro Pro Gly Arg Gln Arg Ala Arg Ser Ser Ser Val
      130      135      140
Pro Arg Glu Val Leu Arg Leu Ser Leu Ser Ser Glu Ser Glu Leu Pro
      145      150      155      160
Ser Leu Pro Leu Phe Ser Glu Lys Ser Lys Thr Thr Lys Asp Ser Pro
      165      170      175
Gln Ala Ala Arg Asp Gly Lys Arg Gly Val Gly Ser Ala Gly Trp Pro
      180      185      190

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Asp Arg Val Thr Phe Arg Gly Gln Tyr Thr Gly His Glu Tyr His Val  
 195 200 205  
 Leu Ser Pro Lys Ala Val Pro Lys Gly Asn Gly Thr Val Ser Cys Pro  
 210 215 220  
 His Cys Arg Pro Ile Arg Thr Gln Asp Ala Gly Gly Ala Val Thr Gly  
 225 230 235 240  
 Asp Pro Leu Gly Pro Pro Ala Asp Thr Leu Gln Cys Pro Leu Cys  
 245 250 255  
 Gly Gln Val Gly Ser Pro Pro Glu Ala Asp Gly Pro Gly Ser Ala Thr  
 260 265 270  
 Ser Gly Ala Glu Lys Ala Thr Thr Arg Arg Lys Ala Pro Ser Thr Pro  
 275 280 285  
 Ser Pro Lys Gln Arg Ser Lys Gln Ala Gly Ser Ser Pro Arg Pro Pro  
 290 295 300  
 Pro Gly Leu Trp Tyr Leu Ala Thr Ala Pro Pro Ala Pro Ala Pro Pro  
 305 310 315 320  
 Ala Phe Ala Tyr Thr Pro Val Pro Pro His His Ala Leu Ser Thr Cys  
 325 330 335  
 Arg Cys Val Leu Cys Ala Cys Arg Thr Tyr Leu Arg Lys Thr Gln Leu  
 340 345 350  
 Pro Ser Gly Arg Pro Gln Pro Leu Pro His Gln Pro Gly Asp Thr Gly  
 355 360 365  
 Thr Pro Ser Ser Ser Thr Trp Ala Thr  
 370 375 377

<210> 216  
 <211> 129  
 <212> PRT  
 <213> Homo sapiens

<400> 216  
 Met Ile Ser Arg Asp His Glu Lys Ser Ala Phe Met Ile Met Val Ser  
 1 5 10 15  
 Pro Leu Pro Val Gly Met Gly Cys Arg Ala Gly Val Asp Thr Glu Glu  
 20 25 30  
 Gln Val Gly Glu Thr Ala Val Ser Gln Ala Arg Pro Thr Glu Ala Gln  
 35 40 45  
 Ala Gly Glu Glu Gly Ala Cys Arg Ser Val Gly Leu Ile Pro Val Tyr  
 50 55 60  
 Val Gln Cys Gly Pro Asp Arg Ile Cys Gly Gln Ser Asp Val Gly Asn  
 65 70 75 80  
 Gln Arg Lys Glu Gly Val Lys Gly Ser Asp Cys Pro Ser Gly Pro Met  
 85 90 95  
 Ala Tyr Gly Val Thr Phe Phe Glu Ile Ser Gly Gly Ser Asn Gly Pro  
 100 105 110  
 Asn Arg Gly Ser Val Gln Gly Thr Leu Lys Ala Gly Cys Leu Ser Val  
 115 120 125  
 Trp  
 129

<210> 217  
 <211> 184  
 <212> PRT  
 <213> Homo sapiens

<400> 217  
 Met Gly Ser Arg Phe Ile Glu Val Met Gln Gly Ser Glu Gln Gln Trp  
 1 5 10 15  
 Ile Glu Phe Gly Gly Asn Ala Val Lys Glu Gly Asp Val Leu Arg Arg

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      20      25      30
Ser Glu Glu His Ser Pro Pro Arg Gly Ile Asn Asp Arg His Phe Arg
      35      40      45
Lys Arg Ser His Ser Lys Ser Pro Arg Arg Thr Arg Ser Arg Ser Pro
      50      55      60
Leu Gly Phe Tyr Val His Leu Lys Asn Leu Ser Leu Ser Ile Asp Glu
      65      70      75      80
Arg Asp Leu Arg Asn Phe Phe Arg Gly Thr Asp Leu Thr Asp Glu Gln
      85      90      95
Ile Arg Phe Leu Tyr Lys Asp Glu Asn Arg Thr Arg Tyr Ala Phe Val
      100      105      110
Met Phe Lys Thr Leu Lys Asp Tyr Asn Thr Ala Leu Ser Leu His Lys
      115      120      125
Thr Val Leu Gln Tyr Arg Pro Val His Ile Asp Pro Ile Ser Arg Lys
      130      135      140
Gln Met Leu Lys Phe Ile Ala Arg Phe Leu Tyr Lys Ile Gln Ala Leu
      145      150      155      160
Gln Lys Ile Ala Arg Thr Val His Lys Asn Thr Leu Lys Lys Val Thr
      165      170      175
Leu Ala Arg Asn Cys Ala Ser Ile
      180      184

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<210> 218  
 <211> 149  
 <212> PRT  
 <213> Homo sapiens

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      <400> 218
Met Ala Ala Asp Gly Glu Arg Ser Pro Leu Leu Ser Glu Pro Ile Asp
      1      5      10      15
Gly Gly Ala Gly Gly Asn Gly Leu Val Gly Pro Gly Gly Ser Gly Ala
      20      25      30
Gly Pro Gly Gly Gly Leu Thr Pro Ser Ala Pro Pro Tyr Gly Ala Gly
      35      40      45
Lys His Ala Pro Pro Gln Gly Lys Pro Gly Arg Val Arg Gly Ala Pro
      50      55      60
Arg Gly Thr Leu Lys Ala Gly Glu Gly Ala Gly Pro Arg Ala Glu Ala
      65      70      75      80
Gly Pro Ser Arg Gln Val Arg Asp Cys Cys Thr Cys Asp Trp Ala Arg
      85      90      95
Leu Pro Ser Leu Arg Asn Arg Asp His Ser Leu Gly Thr Glu Gly Gly
      100      105      110
Ser Glu Gln Pro Asp Arg Ser Ala Asn Tyr Glu Lys Pro Ser Glu Leu
      115      120      125
Gly Gln Arg Val Glu Asp Gln Lys Asp Phe Pro Thr Thr Val Glu His
      130      135      140
Gln Trp Gly Cys Lys
      145      149

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<210> 219  
 <211> 79  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 219
Met Asp Glu Pro Asp His Gln Pro Trp Lys Ser His Ser Ala Ser Trp
      1      5      10      15
Val Leu Lys His Gln Arg Ala Tyr Ile Tyr Thr Leu Thr Phe Ser Val
      20      25      30

```

Thr Leu His Ile Phe Asn Cys Val Arg Gln Lys Phe Ser Ala Leu Phe  
                   35                  40                  45  
 Gly Ser Pro Thr Leu Cys Pro Ala Pro Leu Phe Gly Leu Gly Thr Pro  
           50                  55                  60  
 Ala Ser Ser Thr Pro Ala Lys Ser Glu Trp His Thr Leu Phe Leu  
   65                  70                  75                  79

<210> 220  
 <211> 46  
 <212> PRT  
 <213> Homo sapiens

<400> 220  
 Met Ile Gln Ser Arg Val Cys Leu Gly Gly Glu Asn Arg Ala Leu Arg  
   1                  5                  10                  15  
 Gly Ser Ala Leu Cys Ser Pro Ala Ala Gly Thr Ser Ala Gly Thr  
           20                  25                  30  
 Gly Thr Ala Asp Thr Ala Pro Gly Val Gly Gly Ala Thr Lys  
           35                  40                  45  46

<210> 221  
 <211> 68  
 <212> PRT  
 <213> Homo sapiens

<400> 221  
 Met Gly Asp Glu Asp Lys Arg Ile Thr Tyr Asp Asp Ser Glu Pro Cys  
   1                  5                  10                  15  
 Thr Gly Met Asn Tyr Thr Pro Ser Met His Gln Glu Ala Gln Glu Glu  
           20                  25                  30  
 Thr Leu Met Lys Leu Lys Gly Ile Asp Ala Asn Glu Pro Ser Glu Gly  
           35                  40                  45  
 Cys Ile Leu Leu Lys Ser Ser Glu Lys Lys Leu Gln Glu Thr Pro Thr  
   50                  55                  60  
 Glu Ala Asn His  
   65                  68

<210> 222  
 <211> 95  
 <212> PRT  
 <213> Homo sapiens

<400> 222  
 Met Tyr Ala Leu Pro Ile Pro Ile Gln Tyr Tyr Thr Lys Arg Ser Ser  
   1                  5                  10                  15  
 Arg Arg Pro Lys Lys Ser Gly Tyr Lys Arg Gln Pro Asn Gln Lys Glu  
           20                  25                  30  
 Ile Lys Leu Ser Leu Phe Thr Glu Met Ile Thr Arg Val Asp Lys Asn  
           35                  40                  45  
 Gln Ser Ser Phe Ser Ile Arg Ala Leu Ile Asn Leu Lys Pro Lys Phe  
   50                  55                  60  
 Ile Phe Lys Met Pro Val Cys Asn Ser Ser Lys Thr Tyr Leu Asp Ile  
   65                  70                  75                  80  
 His Ile His Lys Arg Cys Ile Cys Leu Leu Lys Ser Ile Lys Gly  
                   85                  90                  95

<210> 223  
 <211> 989  
 <212> PRT  
 <213> Homo sapiens

<400> 223  
 Met Leu Asn Ser Arg Asn Asn Phe Ile Arg Asn Tyr Leu Ser Val Ser  
 1 5 10 15  
 Leu Ser Glu His His Met Ala Thr Leu Ala Ser Ile Ile Lys Glu Val  
 20 25 30  
 Asp Lys Asp Gly Leu Lys Gly Ser Ser Asp Glu Glu Phe Ala Ala Ala  
 35 40 45  
 Leu Tyr His Phe Asn His Ser Leu Val Thr Ser Asp Leu Gln Ser Pro  
 50 55 60  
 Asn Leu Gln Asn Thr Leu Leu Gln Gln Leu Gly Val Ala Pro Phe Ser  
 65 70 75 80  
 Glu Gly Pro Trp Pro Leu Tyr Ile His Pro Gln Ser Leu Ser Val Leu  
 85 90 95  
 Ser Arg Leu Leu Ile Trp Gln His Lys Ala Ser Ala Gln Gly Asp  
 100 105 110  
 Pro Asp Val Pro Glu Cys Leu Lys Val Trp Asp Arg Phe Leu Ser Thr  
 115 120 125  
 Met Lys Gln Asn Ala Leu Gln Gly Val Val Pro Ser Glu Thr Glu Asp  
 130 135 140  
 Leu Asn Val Glu His Leu Gln Met Leu Leu Leu Ile Phe His Asn Phe  
 145 150 155 160  
 Thr Glu Thr Gly Arg Arg Ala Ile Leu Ser Leu Phe Val Gln Ile Ile  
 165 170 175  
 Gln Glu Leu Ser Val Asn Met Asp Ala Gln Met Arg Phe Val Pro Leu  
 180 185 190  
 Ile Leu Ala Arg Leu Leu Leu Ile Phe Asp Tyr Leu Leu His Gln Tyr  
 195 200 205  
 Ser Lys Ala Pro Val Tyr Leu Phe Glu Gln Val Gln His Asn Leu Leu  
 210 215 220  
 Ser Pro Pro Phe Gly Trp Ala Ser Gly Ser Gln Asp Ser Asn Ser Arg  
 225 230 235 240  
 Arg Ala Thr Thr Pro Leu Tyr His Gly Phe Lys Glu Val Glu Glu Asn  
 245 250 255  
 Trp Ser Lys His Phe Ser Ser Asp Ala Val Pro His Pro Arg Phe Tyr  
 260 265 270  
 Cys Val Leu Ser Pro Glu Ala Ser Glu Asp Asp Leu Asn Arg Leu Asp  
 275 280 285  
 Ser Val Ala Cys Asp Val Leu Phe Ser Lys Leu Val Lys Tyr Asp Glu  
 290 295 300  
 Leu Tyr Ala Ala Leu Thr Ala Leu Leu Ala Ala Gly Ser Gln Leu Asp  
 305 310 315 320  
 Thr Val Arg Arg Lys Glu Asn Lys Asn Val Thr Ala Leu Glu Ala Cys  
 325 330 335  
 Ala Leu Gln Tyr Tyr Phe Leu Ile Leu Trp Arg Ile Leu Gly Ile Leu  
 340 345 350  
 Pro Pro Ser Lys Thr Tyr Ile Asn Gln Leu Ser Met Asn Ser Pro Glu  
 355 360 365  
 Met Ser Glu Cys Asp Ile Leu His Thr Leu Arg Trp Ser Ser Arg Leu  
 370 375 380  
 Arg Ile Ser Ser Tyr Val Asn Trp Ile Lys Asp His Leu Ile Lys Gln  
 385 390 395 400  
 Gly Met Lys Ala Glu His Ala Ser Ser Leu Leu Glu Leu Ala Ser Thr  
 405 410 415  
 Thr Lys Cys Ser Ser Val Lys Tyr Asp Val Glu Ile Val Glu Glu Tyr  
 420 425 430  
 Phe Ala Arg Gln Ile Ser Ser Phe Cys Ser Ile Asp Cys Thr Thr Ile  
 435 440 445

Leu Gln Leu His Glu Ile Pro Ser Leu Gln Ser Ile Tyr Thr Leu Asp  
 450 455 460  
 Ala Ala Ile Ser Lys Val Gln Val Ser Leu Asp Glu His Phe Ser Lys  
 465 470 475 480  
 Met Ala Ala Glu Thr Asp Pro His Lys Ser Ser Glu Ile Thr Lys Asn  
 485 490 495  
 Leu Leu Pro Ala Thr Leu Gln Leu Ile Asp Thr Tyr Ala Ser Phe Thr  
 500 505 510  
 Arg Ala Tyr Leu Leu Gln Asn Phe Asn Glu Glu Gly Thr Thr Glu Lys  
 515 520 525  
 Pro Ser Lys Glu Lys Leu Gln Gly Phe Ala Ala Val Leu Ala Ile Gly  
 530 535 540  
 Ser Ser Arg Cys Lys Ala Asn Thr Leu Gly Pro Thr Leu Val Gln Asn  
 545 550 555 560  
 Leu Pro Ser Ser Val Gln Thr Val Cys Glu Ser Trp Asn Asn Ile Asn  
 565 570 575  
 Thr Asn Glu Phe Pro Asn Ile Gly Ser Trp Arg Asn Leu Ala Phe Ala  
 580 585 590  
 Asn Asp Pro Ile Pro Ser Glu Ser Tyr Ile Ser Ala Val Gln Ala Ala  
 595 600 605  
 His Leu Gly Thr Phe Cys Ser Gln Ser Leu Pro Leu Ala Ala Ser Leu  
 610 615 620  
 Lys His Thr Leu Leu Ser Leu Val Arg Leu Thr Gly Asp Phe Ile Val  
 625 630 635 640  
 Trp Ser Asp Glu Met Asn Pro Pro Gln Val Ile Arg Thr Leu Val Pro  
 645 650 655  
 Phe Phe Leu Glu Ser Ser Thr Glu Ser Val Ala Glu Ile Ser Ser Asn  
 660 665 670  
 Ser Leu Glu Arg Ile Leu Gly Pro Ala Glu Ser Asp Glu Phe Leu Ala  
 675 680 685  
 Arg Val Tyr Glu Lys Leu Ile Thr Gly Cys Tyr Asn Ile Leu Ala Asn  
 690 695 700  
 His Ala Asp Pro Asn Ser Gly Val Asp Glu Ser Ile Leu Glu Glu Cys  
 705 710 715 720  
 Leu Gln Tyr Leu Glu Lys Gln Leu Glu Ser Ser Gln Ala Arg Lys Thr  
 725 730 735  
 Met Glu Glu Cys Phe Ser Asp Ser Gly Glu Leu Val Gln Ile Met Met  
 740 745 750  
 Ala Thr Ala Asn Glu Asn Leu Ser Ala Lys Phe Cys Asn Arg Val Leu  
 755 760 765  
 Lys Phe Phe Thr Lys Leu Phe Gln Leu Thr Glu Lys Ser Pro Asn Pro  
 770 775 780  
 Ser Leu Leu His Leu Cys Gly Ser Leu Ala Gln Leu Ala Cys Val Glu  
 785 790 795 800  
 Pro Val Arg Leu Gln Ala Trp Leu Thr Arg Met Thr Thr Ser Pro Pro  
 805 810 815  
 Lys Asp Ser Asp Gln Leu Asp Val Ile Gln Glu Asn Arg Gln Leu Leu  
 820 825 830  
 Gln Leu Leu Thr Thr Tyr Ile Val Arg Glu Asn Ser Gln Val Gly Glu  
 835 840 845  
 Gly Val Cys Ala Val Leu Leu Gly Thr Leu Thr Pro Met Ala Thr Glu  
 850 855 860  
 Met Leu Ala Asn Gly Asp Gly Thr Gly Phe Pro Glu Leu Met Val Val  
 865 870 875 880  
 Met Ala Thr Leu Ala Ser Ala Gly Gln Gly Ala Gly His Leu Gln Leu  
 885 890 895  
 His Asn Ala Ala Val Asp Trp Leu Ser Arg Cys Lys Lys Tyr Leu Ser  
 900 905 910  
 Gln Lys Asn Val Val Glu Lys Leu Asn Ala Asn Val Met His Gly Lys  
 915 920 925  
 His Val Met Ile Leu Glu Cys Thr Cys His Ile Met Ser Tyr Leu Ala  
 930 935 940  
 Asp Val Thr Asn Ala Leu Ser Gln Ser Asn Gly Gln Gly Pro Ser His



945                      950                      955                      960  
 Leu Ser Val Asp Gly Glu Glu Arg Ala Ile Glu Val Asp Ser Asn Trp  
                          965                      970                      975  
 Gly Gly Gly Cys Cys Gly Gly Arg Gly Arg Phe Pro Gly  
                          980                      985                      989

<210> 224  
 <211> 237  
 <212> PRT  
 <213> Homo sapiens

<400> 224  
 Met Leu Leu Phe Leu Asn Glu Lys Asn Lys Leu Ile Glu Asn Leu Asn  
   1                  5                  10                  15  
 Leu Ser Leu Lys Thr Lys Lys Pro Leu Phe His Cys Leu Lys Glu Glu  
                   20                  25                  30  
 Lys Ser Gln Met Ala Cys Pro Asp Glu Asn Val Ser Ser Gly Glu Leu  
                   35                  40                  45  
 Arg Gly Leu Cys Ala Ala Pro Arg Glu Glu Lys Glu Arg Glu Thr Glu  
                   50                  55                  60  
 Ala Ala Gln Met Glu His Gln Lys Glu Arg Asn Ser Phe Glu Glu Arg  
                   65                  70                  75                  80  
 Ile Gln Ala Leu Glu Glu Asp Leu Arg Glu Lys Glu Arg Glu Ile Ala  
                   85                  90                  95  
 Thr Glu Lys Lys Asn Ser Leu Lys Arg Asp Lys Ala Ile Gln Gly Leu  
                   100                  105                  110  
 Thr Met Ala Leu Lys Ser Lys Glu Lys Lys Val Glu Gly Ser Ser Ser  
                   115                  120                  125  
 Glu Ile Glu Lys Leu Ser Ala Ala Phe Ala Lys Ala Arg Glu Ala Leu  
                   130                  135                  140  
 Gln Arg Ala Gln Ser Gln Glu Phe Gln Gly Cys Glu Asp Tyr Glu Thr  
                   145                  150                  155                  160  
 Ala Leu Ser Gly Lys Glu Ala Leu Ser Ala Gly Val Arg Ser Gln Ser  
                   165                  170                  175  
 Leu Thr Lys Ser Ser Glu Pro His Arg Leu Arg Arg Ser Ile Lys Lys  
                   180                  185                  190  
 Ile Thr Gln Glu Leu Ser Asp Leu Gln Gln Glu Arg Glu Arg Leu Glu  
                   195                  200                  205  
 Lys Asp Leu Glu Gln Ala His Arg Lys Asn Ser Lys Gly Val Cys Thr  
                   210                  215                  220  
 Ile Arg Asp Leu Arg Asn Glu Val Gln Asn Thr Arg Asn  
                   225                  230                  235                  237

<210> 225  
 <211> 194  
 <212> PRT  
 <213> Homo sapiens

<400> 225  
 Met Pro Asn Val Leu Leu Pro Pro Lys Glu Ser Asn Leu Phe Lys Arg  
   1                  5                  10                  15  
 Ile Leu Lys Cys Tyr Asp His Asn Gln Ser Thr Thr Gly Leu Gln Phe  
                   20                  25                  30  
 Ser Gln Thr Ile Leu Pro His Leu Lys Phe Ala Glu His Gly Glu Thr  
                   35                  40                  45  
 Leu Ala Met Lys Gly Leu Thr Leu Asn Cys Leu Gly Lys Lys Glu Glu  
                   50                  55                  60  
 Ala Tyr Glu Phe Val Arg Lys Gly Leu Arg Asn Asp Val Lys Ser His  
                   65                  70                  75                  80

Val Cys Trp His Val Tyr Gly Leu Leu Gln Arg Ser Asp Lys Lys Tyr  
                             85                            90                            95  
 Asp Glu Ala Ile Lys Cys Tyr Arg Asn Ala Leu Lys Leu Asp Lys Asp  
                             100                            105                            110  
 Asn Leu Gln Ile Leu Arg Asp Leu Ser Leu Leu Gln Ile Gln Met Arg  
                             115                            120                            125  
 Asp Leu Glu Gly Tyr Arg Glu Thr Arg Tyr Gln Leu Leu Gln Leu Arg  
                             130                            135                            140  
 Pro Thr Gln Arg Ala Ser Trp Ile Gly Tyr Ala Ile Ala Tyr His Leu  
                             145                            150                            155                            160  
 Leu Lys Asp Tyr Asp Met Ala Leu Asn Ser Ser Lys Arg Asn Pro Val  
                             165                            170                            175  
 His Val Trp Gly Thr Thr Gly Asn Pro Trp Trp Val His Lys Arg Ser  
                             180                            185                            190  
 Phe Arg  
                             194

<210> 226  
 <211> 188  
 <212> PRT  
 <213> Homo sapiens

<400> 226  
 Met Gly Thr Glu Lys Phe Pro Lys Glu Leu Glu Asn Lys Lys Lys Glu  
   1                            5                            10                            15  
 Leu His Phe Leu Gln Lys Val Val Ser Glu Pro Ala Met Gly His Ser  
                             20                            25                            30  
 Asp Leu Leu Glu Leu Glu Ser Lys Ile Asn Glu Ile Asn Thr Glu Ile  
                             35                            40                            45  
 Asn Gln Leu Ile Glu Lys Lys Met Met Lys Asn Glu Pro Ile Glu Gly  
                             50                            55                            60  
 Lys Leu Leu Leu Tyr Arg Gln Gln Ala Ser Ile Ile Ser Arg Lys Lys  
                             65                            70                            75                            80  
 Glu Ala Lys Ala Glu Glu Leu Gln Glu Ala Lys Glu Lys Leu Ala Ser  
                             85                            90                            95  
 Leu Glu Arg Glu Ala Ser Val Lys Arg Asn Gln Thr Arg Glu Phe Asp  
                             100                            105                            110  
 Gly Thr Glu Val Leu Lys Gly Asp Glu Phe Lys Arg Tyr Val Asn Lys  
                             115                            120                            125  
 Leu Arg Ser Lys Ser Thr Val Phe Lys Lys Lys His Gln Ile Ile Ala  
                             130                            135                            140  
 Glu Leu Lys Ala Glu Phe Gly Leu Leu Gln Arg Thr Glu Glu Leu Leu  
                             145                            150                            155                            160  
 Lys Gln Arg His Glu Asn Ile Gln Gln Gln Leu Gln Thr Met Glu Glu  
                             165                            170                            175  
 Lys Lys Gly Ile Ser Gly Tyr Ser Tyr Ile Pro Arg  
                             180                            185                            188

<210> 227  
 <211> 1220  
 <212> DNA  
 <213> Homo sapiens

<400> 227  
 ggaccaaga gatagcatct agggattcag ggggtccagg gttagaagct gatacaacag 60  
 ggatccagggt gaaagagggt gggggttcag aggttccaga gatagcgact gggacagcag 120  
 aaactgagat attggggacc caagagatag catctaggag ttcaggggtc ccagggctag 180  
 aatctgaggt agctggggcc caggagacag aggtcggggg ttcagggatc tcagggccc 240  
 aggttggaat ggcagaggcc cgagtactga tgaccgtaa gacagaaatt atagttccag 300

aggctgagaa	ggaagaggct	cagacttcgg	gggtccagga	agcagagact	agagttggga	360
gtgctctcaa	atatgaggct	ttaagggccc	cagtcactca	gccaagagtt	ttaggatccc	420
aggaagcaaa	agcagagatt	tcaggagtac	aagggtcaga	gactcaagtt	ctgagagtcc	480
aggaggcaga	ggctgggggt	tgggggatgt	cagagggcaa	atctggggct	tggggggccc	540
aggaagcaga	gatgaagggt	ttagagtctc	cagagaacaa	atctgggtact	tttaaggccc	600
aggaagcaga	ggctgggggt	ttgggaaatg	agaaggggaa	agaagctgag	ggaagcctca	660
cagaggccag	cctgcctgaa	gcacagggtg	ccagtggggc	aggggctggg	gcgcccaggg	720
cctcttcccc	agagaaggct	gaagaggaca	ggaggctgcc	gggcagccag	gcaccacctg	780
ccctggctcag	ctccagccag	tccctgctgg	agtggtgcca	ggaagtcacc	actggctacc	840
gtggcgctccg	catcaccaac	ttcaccacat	cctggcgcaa	cggcttggtc	ttctgtgcca	900
tctgcaccg	attctaccca	gacaagattg	actatgcccc	gctagacca	ctcaacatca	960
agcagaacaa	caagcaggcc	ttcgatggct	tcgcggctct	gggcgtgtcg	cggctgtctg	1020
agcccgcgga	catggtgcta	ctgtcgggtc	ccgacaagct	catcgctcatg	acgtacctgt	1080
gccagatccg	cgccttctgc	accgggcagg	agctgcagct	ggtacaactg	gagggcgggc	1140
gcggcgcccg	cacgtaccgc	gtgggcagcg	cccagcccag	cccgccttc	cccgtatagg	1200
gcagggcgga	tccccgacct					1220

<210> 228  
 <211> 808  
 <212> DNA  
 <213> Homo sapiens

<400> 228	
gtaccgcttc	ggaatttccg
gtgtgggtac	tgtgtctgtg
ggcggagaa	cgacgaaagg
gtagtgttac	gggtgcggcc
gttcagggtg	tggacgagcg
cctggcctga	aatgggggtg
tttgtctttg	accgggtctt
acgcacagcg	tcttgacag
gccaccgggg	ctgggaagac
tacctgacca	ccgtggaact
gaggtgtctc	tcagctacca
aaggggcccc	ttgccatccg
ttccaccagc	cagcctcagc
cgcacgcagc	acccactga
ggcgacgat	ttcgtggagg
gtgtggggcg	ctctctcccc
cgacgccagc	
cacgctgcaa	
gcggccagtg	
tggagggttc	
agacctgacg	
ccagcacacc	
tgcctacggg	
cggcatcatg	
gaagcacttc	
cctggagccc	
aggactttct	
gaaccgtaac	
808	

<210> 229  
 <211> 659  
 <212> DNA  
 <213> Homo sapiens

<400> 229	
aggcagagcc	aagtgcgtcc
ttgggtggaag	aagacagcag
tttaagaaagg	aattctagca
aaatatattg	gtgcaagtcc
cttaccacaga	cctgggtcatc
agctacagaa	aactcagaga
tattaaactc	aggaggagga
cagagatggg	actggattta
aggctttctt	tgagactaag
gtggggatcc	tttctttaa
cattatactg	tagatctggc
ccccgttgcg	aaggtctttc
ttcactgtgc	tggtgggaag
gtaaatacaa	cagaatcagt
ctccctgggt	gtgtatccat
gggagaagaa	aacagaaaaa
tatacgggcc	gcgtgtgctt
caacagggat	gagcgtccca
tattcagtat	ccatattttgc
tatttttgtt	aaatcttgga
catttgcagc	cttagttctt
acgcggccg	
659	

<210> 230  
 <211> 460  
 <212> DNA  
 <213> Homo sapiens

<400> 230  
 tttcgtgtcc ttgccccag cctgggactc cggagttgcg tttctaccgc tgcttcaggg 60  
 tctagcccag ccgaatccgc gtccggctgt aactcgagtg ccagtttcag ctgtgagttc 120  
 aacatggagg caaatcagtg ccccttggtt gtggaacat cttaccaga cctggtcac 180  
 aatgtaggag aagtgactct tggagaagaa aacagaaaa agctgcagaa aattcagaga 240  
 gaccaagaga aggagagagt tatgctgggt gcatgtgctt tattaaactc aggaggagga 300  
 gtgattcgaa tggccaagaa ggttgagcat accgtggaga tgggactgga tttagaacag 360  
 tctttgagag agcttattca gtcttcagat ctgcaggctt tctttgagac caagcaacaa 420  
 ggaaggtggt tttacatttt tgttaaactc tggagcagtg 460

<210> 231  
 <211> 1151  
 <212> DNA  
 <213> Homo sapiens

<400> 231  
 tttcgttcgg aattgtgggc gactcggcta atggcgctcg cgagtcttag gggcctgggg 60  
 agctggcgct gaagcttctt gccagggttg ctggtgacac ccggtgtggc tgggccccgc 120  
 ggcagcggag ggacctgccc gccttgtggg tttctcggcc agagtccggc gaggctagcg 180  
 ggacgggtgc actgcggggg gcgcctccga gaaaagccag aggtgttgcg gggaagctgc 240  
 tgggggacgc tcgagcaggc tccgggttcg cagcccaggg cccaagaagc gggctgtga 300  
 aggaccagag acaccgggag ggagctgcct gtggccctaa ggagctgacc gtgccagagc 360  
 ttgtttgtac ctctcgaaa ttggctggga ccttgaggga tcatgtccgg caccagcagc 420  
 cccgagcgcg tgaagaagct gctggagaat atgcagagcg acttgccgcg cttgtcactg 480  
 gagtgcaga agaaattccc acctgtcaaa gaggctgtcg aatcaggaat aataaaagt 540  
 aaaacaattg ctgcacgaaa cactgaaatt ttggcagcac tgaaagagaa cagctcagag 600  
 ggtgtacagc cttttttaat gggttgtgga accaaggac cgaagatcac tcagctatgt 660  
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<210> 232  
 <211> 722  
 <212> DNA  
 <213> Homo sapiens

<400> 232  
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<211> 768
<212> DNA
<213> Homo sapiens
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<400> 233						
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<211> 939
<212> DNA
<213> Homo sapiens
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<400> 234						
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 <211> 681  
 <212> DNA  
 <213> Homo sapiens

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 aaaagaaaca aacccaatg ggatttggat gatgaaatcc tgcagttgga aacacctcct 300  
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<210> 236  
 <211> 544  
 <212> DNA  
 <213> Homo sapiens

<400> 236  
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 tgac 544

<210> 237  
 <211> 584  
 <212> DNA  
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<220>  
 <221> misc\_feature  
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 <223> n = a,t,c or g

<400> 237  
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 <212> DNA  
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 <212> DNA  
 <213> Homo sapiens

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<210> 240  
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 <212> DNA  
 <213> Homo sapiens

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<210> 241  
 <211> 265  
 <212> DNA  
 <213> Homo sapiens

<400> 241  
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 ccacaagtac caccctgaag gcctccgaga agtctacaat ggaacagttg gtggaaaaag 180  
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<210> 242  
 <211> 724  
 <212> DNA  
 <213> Homo sapiens

<220>  
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 <223> n = a,t,c or g

<400> 242  
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<210> 243  
 <211> 1129  
 <212> DNA  
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<210> 244  
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 <212> DNA  
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<400> 244						
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<210> 245  
 <211> 760  
 <212> DNA  
 <213> Homo sapiens

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<210> 246  
 <211> 582  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 246

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&lt;210&gt; 247

&lt;211&gt; 814

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 247

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&lt;210&gt; 248

&lt;211&gt; 794

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (794)

&lt;223&gt; n = a,t,c or g

&lt;400&gt; 248

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 <212> DNA  
 <213> Homo sapiens

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 <212> DNA  
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&lt;210&gt; 255

&lt;211&gt; 2862

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 255

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 <212> DNA  
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<400> 256

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;211&gt; 2647

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 261

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 262

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&lt;211&gt; 2006

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;223&gt; n = a,t,c or g

&lt;400&gt; 266

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&lt;210&gt; 278

&lt;211&gt; 1729

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

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&lt;211&gt; 6815

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 279

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&lt;210&gt; 280

&lt;211&gt; 1977

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

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&lt;210&gt; 281

&lt;211&gt; 1231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 281

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&lt;210&gt; 285

&lt;211&gt; 3009

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

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 <213> Homo sapiens



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 <212> DNA  
 <213> Homo sapiens

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 <212> DNA  
 <213> Homo sapiens

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 <211> 3963  
 <212> DNA  
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&lt;210&gt; 297

&lt;211&gt; 3010

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 297

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&lt;210&gt; 298

&lt;211&gt; 3994

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 298

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&lt;210&gt; 299

&lt;211&gt; 2851

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 299

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&lt;213&gt; Homo sapiens

&lt;400&gt; 303

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WO 01/53453

1924

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&lt;211&gt; 1918

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 309

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&lt;211&gt; 333

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

&lt;400&gt; 321

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 327

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 329

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&lt;213&gt; Homo sapiens

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 gcttccatgt gccaaaggca agggcagtg cagtgcactgc caaaagcaag ccaagcaaga 900  
 agcagcagat acatctctta cgtgggtatc tgcgccaat agatgacact ttctgagc 960  
 gaggacaacg tgccaaagtg cggctctgtg actctgtcca cagaaaagta ttcttgcaat 1020  
 gtccacagat aacctgaca cccatgggtt ggggttctg actcagagg ccggggtgca 1080  
 caggccccag gttgatgatt cttttgcagt agggccagg gcatgcaatc cgttgggatg 1140  
 tcactttgca gataaggaga cagttacagg ggcacgaac atattttth cctgggggtg 1200  
 cattcttgat tggggtggct tcattgcaga caccacattt gactacatgc tgatgcatc 1260  
 tgccttccac gttgatgaga gattggcaga ctggcaggat gatcatagg gactccac 1320  
 tgtccgggct agttaagggt gaatagggg gtgggtctc cccaggcaac acggctggat 1380  
 gccctcggg aaacggggga aatgcggctc cgtacgggtg tgcggagggt gtcaggcctc 1440  
 cccggggccc agccccactc ccgcccggcc ccaactaaac gttgcccgc gcgccacgt 1500  
 cgtggggctc agacagcagc ggggaacgct ctccatctgc cggcatggcc gccaccgccc 1560  
 cctcccgtc aggtcgg 1577

<210> 332  
 <211> 339

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 332

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ggttcaggtc	ttcttgatca	ctttaagaac	gctcgtgaaa	ctgcccaggc	catcaagggg	120
atgcatacgt	gagaagtcac	caagtgtctg	aaagacgtcc	ctttatagaa	acagtgtatg	180
ccattccgac	ttggcagggg	tggagctggc	aggtgtacct	aggccaaaca	gtggggctgg	240
acacaggggt	ggtgacccga	aaagagcgct	gaatttttgc	tgcacacaat	taaaaatgtg	300
gagagtcaca	ctgaatgtga	gggtgtagat	gtaggctct			339

&lt;210&gt; 333

&lt;211&gt; 1058

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 333

agcggcgcgc	caacaaagga	gtcaccgcgc	gatgagcccc	ggcacccccgc	gaccgaccat	60
gggcagatcc	cagggcagcc	caatggatcc	aatggatgatg	aagagacctc	agttgtatgg	120
catgggcagt	aacctcatt	ctcagcctca	gcagagcagt	ccgtaccag	gaggttccta	180
tgccctcca	ggcccacagc	ggtatccaat	tggcatccag	ggtcggactc	ccggggccat	240
ggccggaatg	cagtaccctc	agcagcagat	gccacctcag	tatggacagc	aagggtgtgag	300
tggttactgc	cagcagggcc	aacagccata	ttacagccag	cagccgcagc	ccccgcacct	360
cccaccccag	gcgcagtatc	tgccgtccca	gtcccagcag	aggtaccagc	cgcagcagga	420
catgtctcag	gaaggctatg	gaactagatc	tcaaccttcc	tctggccccc	ggaaaacctta	480
accatgaaga	cttgaacttt	aatacagcaa	gaaagaccat	caagtttacc	agtaagacat	540
tattgtgctg	atttggaaat	gtaatgagtt	aaagactttt	agaaagagct	gttggttttg	600
tttgttctac	tttatattat	gacatgattg	agaagtttct	agacttcagg	tttattttgt	660
ggtcaatttt	tcaaggttta	ccttttagga	gctctgtagt	cctggataag	tctatttcat	720
gtgtatatat	ctctgttgca	gagtgttagac	atcagttgga	aggttttatg	cggctggtcg	780
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ttggcagcga	tacagaacag	aggtgtcctt	agaggagtca	aaacttaaaa	gaaatttgca	900
ctttgcaaag	gatacaaatg	atgagataaa	atacctgata	gtaatttgaa	tttcttctag	960
gactttctat	ttatgtaatg	agaaatcacc	caaaagaagg	tagtttgaaa	tttgagacca	1020
gacgcggtgg	ctcacgcctg	taatcccagc	tctttggg			1058

&lt;210&gt; 334

&lt;211&gt; 754

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (754)

&lt;223&gt; n = a, t, c or g

&lt;400&gt; 334

cttttgaaaa	gcagtgaaaa	aaagctacaa	gaaacaccaa	ctgaagcaaa	tcacgtacaa	60
agactgagac	aaatgctggc	ttgccctcca	catgggtttac	tggacagggg	cataacaaat	120
gttaccatca	ttgttcttct	gtgggctgta	gtttgggtcaa	ttactggcag	tgaatgtctt	180
cctggaggaa	acctatttgg	aattataatc	ctattctatt	gtgccatcat	tgggtggtaaa	240
cttttggggc	ttattaagtt	acctacattg	cctccactgc	cttctcttct	tggcatgctg	300
cttgacaggg	ttctcatcag	aaatatccca	gtcatcaacg	ataatgtgca	gatcaagcac	360
aagtggtctt	cctcttttag	aagcatagcc	ctgtctatca	ttctgggttcg	tgctggcctt	420

ggctctggatt	caaaggccct	gaagaagtta	aaggcggttt	gtgtaagact	gtccatgggt	480
ccctgtattg	tggaggcgtg	cacatctgct	cttcttgccc	attacctgct	gggtttacca	540
tggcaatggg	gatttatact	gnngtaatga	ttgtttcttt	gtcatatgaa	aatatgtagg	600
gacatttagg	gctttccctg	attgcataca	agagaatgca	taatagaatt	ttcttataga	660
tatcagacaa	tgcaacatag	atgttacagc	ataatttaaa	tattctaact	tccaacataa	720
gttatgtggt	aataggcgct	aactcttaca	gcta			754

<210> 335  
 <211> 402  
 <212> DNA  
 <213> Homo sapiens

<400> 335						
tgtgcctggc	atgtcaacat	acttattggt	aaaagactga	atactttccc	atacagatca	60
ggaacaagac	aaggatgtat	gctcttacca	ttcctattca	atactatact	aaaagatcta	120
gtcactgcac	taaaaaatca	ggatataaaa	ggcaaacaaa	tcaaaaagaa	ataaaaactgt	180
ccctttttac	agaaatgatt	acccgtgtag	ataaaaaatca	atcatccttt	tctatacgag	240
cactgattaa	tctaaaacca	aaatttattt	ttaaaatgcc	agtttgcaat	agctctaaaa	300
catacttaga	catacatata	cacaaaaggt	gtatatgtct	gctgaaaagt	ataaaaaggct	360
gatttcacaa	atcaaaaagcc	taaataatac	catgttcatg	ga		402

<210> 336  
 <211> 885  
 <212> DNA  
 <213> Homo sapiens

<400> 336						
tttgggggat	gggactgaga	tagatttccc	ttatttaatt	tttcttccat	cctgcagatt	60
tatgacctgt	gtgttgatgc	cttgagtcca	accttctatt	ttctcctgcc	aagctcaaag	120
ataagagatg	ttaccttcct	tttcaatgag	gagggaaaaga	acatcattgt	tataatgtct	180
tcggctgggt	acatctatac	tcagcttatg	gaagaggcca	gcagtgccca	gcagggaccc	240
ttctatgtca	ctaattgtgt	ggaaatcaat	catgaggacc	tgaaggacag	taacagccag	300
gtggcgggcg	gtggtgtgtc	cgtgtactac	tcccacgtgt	tgcagatggt	gttcttcagc	360
tattgtcaag	gcaaatcatt	cgcagccacc	atcagcagga	caaccctgga	ggtgttgcaa	420
ctcttcccca	tcaacatcaa	aagttccaat	ggtggcagta	agacttctcc	tgtcttttgc	480
cagtggtctg	aggtgatgaa	ccacctggc	ttggtgtgct	gtgtccagca	aactacaggg	540
gtgccgtggg	tagttatggt	gaaaccagac	acttttctta	tccaggagat	taagactctt	600
cctgctaaag	cgaagatcca	agacatggtt	gctattagga	acacggcctg	caatgagcag	660
cagcggacaa	caatgattct	gctgtgcgag	gatggcagcc	tgcgcattta	catggccaac	720
gtggagaaca	cctcctactg	gctgcagcca	tccctgcagc	ccagcagtg	catcagcatc	780
atgaagcctg	ttcgaaagcg	caaaacagct	acaatcacia	cccgcacgtc	tagccagggtg	840
actttcccca	ttgacttttt	tgaacacaac	cagccagtct	caaaa		885

<210> 337  
 <211> 769  
 <212> DNA  
 <213> Homo sapiens

<400> 337						
ccgggaaaaga	tggcggcgct	tgtggtttga	attccagcgg	cgccgccaga	gtctgaacaa	60
gagctgggggt	ggagggggcg	gggacctggg	gagcccgcg	ggtcgctatc	gcggggggta	120



ctagtggcgc	cgccgccaca	gacaccaacg	ccgtcgccac	ctctgtatcc	atgatggact	180
tgggtgttga	agaggacgtc	accgtccctg	ggacgctcag	cggctgcagt	ggccttggtc	240
ccagtgtacc	agatgacctg	gatggcatca	accccaatgc	tgggttggga	aatggctctgc	300
tcccaaatgt	gtcagaagaa	acagtgtctc	ccaccagagc	acggaacatg	aaggactttg	360
aaaatcaa	actgaattg	aagaaagaaa	actttaacct	aaagctccgc	atctatttcc	420
ttgaggaaag	aatgcaacag	gaatttcacg	gccccactga	acatatctac	aaaactaaca	480
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tcatcaaagc	ctcgtgagta	ccatcatccg	ttgaaagctt	gcaagtccgc	cacactgggt	600
tggtcagtga	aatagagccg	tacacttttc	taagacagtt	ggtttccatc	tggactctga	660
ggactgcaag	gagggttttg	tttttactta	attattttact	tttcaacaag	cttttaagat	720
ataccatgct	tatagaaaaa	tgaacagatc	ttaagtgtac	agcgtgaat		769

&lt;210&gt; 338

&lt;211&gt; 633

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

tgccgaacag	ccaggtgcc	caattgcaac	tgtagaccaa	tgaactaatc	catcgccgcg	60
agcccgaactc	tcagcagcgg	ttcgtcccg	tgcccacccc	cgcaagcgg	agcgcgcggg	120
cacctagcct	ccctgccggc	cacctagcct	ccctgccggc	cacgatgccg	aacgtgctgc	180
tgcgcgccaa	ggagagcaac	ctcttcaaac	gcaccttgaa	atgttatgaa	cagaagcagt	240
acaaaaatgg	cctcaagttt	tgcaagatga	ttctgtcgaa	cccaaaat	gctgaacatg	300
gagagacttt	ggctatgaaa	ggattaacac	tgaactgttt	aggaaaaaaa	gaagaagctt	360
atgagtttgt	tcgtaaagga	cttcgtaaatg	atgtcaagag	tcatgtctgt	tggcatgtat	420
atggactctt	gcagcgttct	gataaaaaat	atgatgaagc	tataaaatgt	taccgaaatg	480
ccctcaaatt	agataaagat	aacctgcaaa	ttttgaggga	tctctcactg	ttgcagatcc	540
aatgagaga	ccttgaaggt	taccgagaga	caagatacca	gcttcttcag	ttgcgcccc	600
cacagcgtgc	ctcctggatt	ggatatgcta	ttg			633

&lt;210&gt; 339

&lt;211&gt; 1743

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 339

ctcgaaacgg	cttcgtgagg	agaatttgag	ttaaaattat	aagattttatt	tattattgat	60
caaatataat	tcattatgga	cagtctcaat	aaggagccct	ttaggaagaa	ctataattta	120
atcacgtttg	attccttgga	gccaatgcaa	ctattacaag	ttctcagtga	tgttctggct	180
gagattgacc	caaagcaact	tgtggatatc	agagaggaga	tgccagagca	gacagccaaa	240
cgaatgttga	gccttcttgg	tattcttaag	tacaaacctt	caggaaatgc	cacagatatg	300
agtacttttc	gtcagggttt	ggtgattgga	agtaaacctg	taatttacc	agtgtccac	360
tggcttcttc	agaggactaa	tgaactgaag	aaaagagcat	atttagctcg	ttttttaata	420
aaacttgagg	taccaagtga	gtttcttcag	gatgaaactg	tggctgacac	caataaacag	480
tatgaagagt	taatggaagc	ctttaaaact	ttgcataaag	aatatgagca	gctcaagata	540
tctggatttt	ctacagcaga	aataagaaag	gatatcagtg	caatggaaga	agaaaaggat	600
cagctcatta	agagagtgtga	acatttgaag	aaaagggttg	agacagctca	gaatcatcaa	660
tggatgctta	aaatagcaag	gcaacttcga	gttgaaaaag	agagagaaga	atatcttgca	720
caacagaaac	aggaacaaaa	gaatcagcta	tttcatgcag	tgcaaaagatt	gcaaagagta	780
caaaaaccag	tgaaaagcat	gcgccaagct	gcagcagatg	caaaagcctga	aagttaaatg	840
aagaggctag	aggaggagat	aaaatttaat	ttatatatgg	gaactgaaaa	atttcctaaa	900
gaattagaaa	ataagaaaaa	ggaattacat	tttttcaaaa	aagtagtttc	agagccagct	960
atggggcatt	ctgatcttct	tgaacttgaa	tctaaaataa	atgaaataaa	cacagaaatt	1020
aaccagttga	ttgaaaagaa	aatgatgaga	aatgagccca	ttgaaggcaa	actctcactg	1080
tataggcaac	aggcatctat	cattttcccg	aaaaaagaag	ccaaagctga	ggaacttcag	1140

```

gaggccaagg agaagttagc cagcctagag agagaagcat cagtaaagag aaatcagacc 1200
cgtgaatttg atggtactga agttttaaaag ggagatgagt tcaaacgata tgtcaataaa 1260
cttcgaagca agagtacagt tttcaaaaag aagcatcaga taatagctga acttaaagct 1320
gaattcggtc ttttgcagag gactgaagaa cttcttaagc aacgtcatga aaatattcaa 1380
caacaactgc aaactatgga ggagaaaaag ggtatatctg gatatagtta cacccaagaa 1440
gagctagaaa gagtatctgc actgaagagt gaagttgatg aaatgaaagg acgaacattg 1500
gatgatatgt ctgaaatggt gaaaaaactg tattcattgg tatctgaaaa gaagtcagct 1560
cttgccctcag ttataaaaga gctacgacag ttgcgtcaaa aatatcaaga actgaccag 1620
gagtgatgatg aaaagaaatc ccagtatgat agctgtgcag caggcctcga aagcaatcgg 1680
tccaaattag aacaggaagt tagaagactc cgtgaagaat gtcttcaaga agaaagtaga 1740
tac 1743

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<210> 340  
 <211> 398  
 <212> PRT  
 <213> Homo sapiens

<400> 340

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Thr Gln Glu Ile Ala Ser Arg Asp Ser Gly Val Pro Gly Leu Glu Ala
 1          5          10          15
Asp Thr Thr Gly Ile Gln Val Lys Glu Val Gly Gly Ser Glu Val Pro
          20          25          30
Glu Ile Ala Thr Gly Thr Ala Glu Thr Glu Ile Leu Gly Thr Gln Glu
          35          40          45
Ile Ala Ser Arg Ser Ser Gly Val Pro Gly Leu Glu Ser Glu Val Ala
          50          55          60
Gly Ala Gln Glu Thr Glu Val Gly Gly Ser Gly Ile Ser Gly Pro Glu
          65          70          75          80
Ala Gly Met Ala Glu Ala Arg Val Leu Met Thr Arg Lys Thr Glu Ile
          85          90          95
Ile Val Pro Glu Ala Glu Lys Glu Glu Ala Gln Thr Ser Gly Val Gln
          100          105          110
Glu Ala Glu Thr Arg Val Gly Ser Ala Leu Lys Tyr Glu Ala Leu Arg
          115          120          125
Ala Pro Val Thr Gln Pro Arg Val Leu Gly Ser Gln Glu Ala Lys Ala
          130          135          140
Glu Ile Ser Gly Val Gln Gly Ser Glu Thr Gln Val Leu Arg Val Gln
          145          150          155          160
Glu Ala Glu Ala Gly Val Trp Gly Met Ser Glu Gly Lys Ser Gly Ala
          165          170          175
Trp Gly Ala Gln Glu Ala Glu Met Lys Val Leu Glu Ser Pro Glu Asn
          180          185          190
Lys Ser Gly Thr Phe Lys Ala Gln Glu Ala Glu Ala Gly Val Leu Gly
          195          200          205
Asn Glu Lys Gly Lys Glu Ala Glu Gly Ser Leu Thr Glu Ala Ser Leu
          210          215          220
Pro Glu Ala Gln Val Ala Ser Gly Ala Gly Ala Gly Ala Pro Arg Ala
          225          230          235          240
Ser Ser Pro Glu Lys Ala Glu Glu Asp Arg Arg Leu Pro Gly Ser Gln
          245          250          255
Ala Pro Pro Ala Leu Val Ser Ser Ser Gln Ser Leu Leu Glu Trp Cys
          260          265          270
Gln Glu Val Thr Thr Gly Tyr Arg Gly Val Arg Ile Thr Asn Phe Thr
          275          280          285
Thr Ser Trp Arg Asn Gly Leu Ala Phe Cys Ala Ile Leu His Arg Phe
          290          295          300
Tyr Pro Asp Lys Ile Asp Tyr Ala Pro Leu Asp Pro Leu Asn Ile Lys
          305          310          315          320
Gln Asn Asn Lys Gln Ala Phe Asp Gly Phe Ala Ala Leu Gly Val Ser

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          325          330          335
Arg Leu Leu Glu Pro Ala Asp Met Val Leu Leu Ser Val Pro Asp Lys
          340          345          350
Leu Ile Val Met Thr Tyr Leu Cys Gln Ile Arg Ala Phe Cys Thr Gly
          355          360          365
Gln Glu Leu Gln Leu Val Gln Leu Glu Gly Gly Gly Gly Ala Gly Thr
          370          375          380
Tyr Arg Val Gly Ser Ala Gln Pro Ser Pro Pro Phe Pro Val
385          390          395          398

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<210> 341  
 <211> 235  
 <212> PRT  
 <213> Homo sapiens

```

          <400> 341
Ala Ser Ser Asp Ala Ser Gly Gly Glu Pro Thr Lys Gly Val Thr Thr
  1          5          10          15
Val Met Ala Val Glu Asp Ser Thr Leu Gln Val Val Val Arg Val Arg
          20          25          30
Pro Pro Thr Pro Arg Glu Leu Asp Ser Gln Arg Arg Pro Val Val Gln
          35          40          45
Val Val Asp Glu Arg Val Leu Val Phe Asn Pro Glu Glu Pro Asp Gly
          50          55          60
Gly Phe Pro Gly Leu Lys Trp Gly Gly Thr His Asp Gly Pro Lys Lys
          65          70          75          80
Lys Gly Lys Asp Leu Thr Phe Val Phe Asp Arg Val Phe Gly Glu Ala
          85          90          95
Ala Thr Gln Gln Asp Val Phe Gln His Thr Thr His Ser Val Leu Asp
          100          105          110
Ser Phe Leu Gln Gly Tyr Asn Cys Ser Val Phe Ala Tyr Gly Ala Thr
          115          120          125
Gly Ala Gly Lys Thr His Thr Met Leu Gly Arg Glu Gly Asp Pro Gly
          130          135          140
Ile Met Tyr Leu Thr Thr Val Glu Leu Tyr Arg Arg Leu Glu Ala Arg
          145          150          155          160
Gln Gln Glu Lys His Phe Glu Val Leu Ile Ser Tyr Gln Glu Val Tyr
          165          170          175
Asn Glu Gln Ile His Asp Leu Leu Glu Pro Lys Gly Pro Leu Ala Ile
          180          185          190
Arg Glu Asp Pro Asp Lys Gly Val Val Gln Gly Leu Ser Phe His
          195          200          205
Gln Pro Ala Ser Ala Glu Gln Leu Leu Glu Ile Leu Thr Arg Gly Asn
          210          215          220
Arg Asn Arg Thr Gln His Pro Thr Asp Ala Asn
225          230          235

```

<210> 342  
 <211> 159  
 <212> PRT  
 <213> Homo sapiens

```

          <400> 342
Ile Tyr Trp Cys Lys Phe Asn Met Glu Ala Asn His Cys Ser Leu Gly
  1          5          10          15
Val Tyr Pro Ser Tyr Pro Asp Leu Val Ile Asp Val Gly Glu Val Thr
          20          25          30
Leu Gly Glu Glu Asn Arg Lys Lys Leu Gln Lys Thr Gln Arg Asp Gln
          35          40          45

```

Glu Arg Ala Arg Val Ile Arg Ala Ala Cys Ala Leu Leu Asn Ser Gly  
 50 55 60  
 Gly Gly Val Ile Gln Met Glu Met Ala Asn Arg Asp Glu Arg Pro Thr  
 65 70 75 80  
 Glu Met Gly Leu Asp Leu Glu Glu Ser Leu Arg Lys Leu Ile Gln Tyr  
 85 90 95  
 Pro Tyr Leu Gln Ala Phe Phe Glu Thr Lys Gln His Gly Arg Cys Phe  
 100 105 110  
 Tyr Ile Phe Val Lys Ser Trp Ser Gly Asp Pro Phe Leu Lys Asp Gly  
 115 120 125  
 Ser Phe Asn Ser Arg Ile Cys Ser Leu Ser Ser Ser Leu Tyr Cys Arg  
 130 135 140  
 Ser Gly Thr Ser Val Leu His Met Asn Ser Arg Ser Thr Arg Pro  
 145 150 155 159

&lt;210&gt; 343

&lt;211&gt; 153

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 343

Phe Arg Val Leu Ala Pro Ser Leu Gly Leu Arg Ser Cys Val Ser Thr  
 1 5 10 15  
 Arg Ala Ser Gly Ser Ser Pro Ala Glu Ser Ala Ser Gly Cys Asn Ser  
 20 25 30  
 Ser Ala Ser Phe Ser Cys Glu Phe Asn Met Glu Ala Asn Gln Cys Pro  
 35 40 45  
 Leu Val Val Glu Pro Ser Tyr Pro Asp Leu Val Ile Asn Val Gly Glu  
 50 55 60  
 Val Thr Leu Gly Glu Glu Asn Arg Lys Lys Leu Gln Lys Ile Gln Arg  
 65 70 75 80  
 Asp Gln Glu Lys Glu Arg Val Met Arg Ala Ala Cys Ala Leu Leu Asn  
 85 90 95  
 Ser Gly Gly Gly Val Ile Arg Met Ala Lys Lys Val Glu His Thr Val  
 100 105 110  
 Glu Met Gly Leu Asp Leu Glu Gln Ser Leu Arg Glu Leu Ile Gln Ser  
 115 120 125  
 Ser Asp Leu Gln Ala Phe Phe Glu Thr Lys Gln Gln Gly Arg Cys Phe  
 130 135 140  
 Tyr Ile Phe Val Lys Ser Trp Ser Ser  
 145 150 153

&lt;210&gt; 344

&lt;211&gt; 180

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 344

Pro Cys Gln Ser Leu Phe Val Pro Leu Gly Asn Trp Leu Gly Pro Trp  
 1 5 10 15  
 Arg Ile Met Ser Gly Thr Ser Ser Pro Glu Ala Val Lys Lys Leu Leu  
 20 25 30  
 Glu Asn Met Gln Ser Asp Leu Arg Ala Leu Ser Leu Glu Cys Lys Lys  
 35 40 45  
 Lys Phe Pro Pro Val Lys Glu Ala Ala Glu Ser Gly Ile Ile Lys Val  
 50 55 60  
 Lys Thr Ile Ala Ala Arg Asn Thr Glu Ile Leu Ala Ala Leu Lys Glu  
 65 70 75 80  
 Asn Ser Ser Glu Gly Val Gln Pro Phe Leu Met Gly Cys Gly Thr Lys

```

      85      90      95
Glu Pro Lys Ile Thr Gln Leu Cys Leu Ala Ala Ile Gln Arg Leu Met
      100      105      110
Ser His Glu Val Val Ser Glu Thr Ala Ala Gly Asn Ile Ile Asn Met
      115      120      125
Leu Trp Gln Leu Met Glu Asn Ser Leu Glu Glu Leu Lys Leu Leu Gln
      130      135      140
Thr Val Leu Val Leu Leu Thr Thr Asn Thr Val Val His Asp Glu Ala
      145      150      155      160
Leu Ser Lys Val Gly Lys Leu Phe Ala Arg Val His Met Cys Phe Glu
      165      170      175
Thr Val Phe Glu
      180

```

<210> 345  
 <211> 70  
 <212> PRT  
 <213> Homo sapiens

```

    <400> 345
Ala Met Ser Pro Pro Thr Val Pro Pro Met Gly Val Asp Gly Val Ser
  1      5      10      15
Ala Tyr Leu Met Lys Lys Arg His Thr His Arg Lys Gln Arg Arg Lys
      20      25      30
Pro Thr Phe Leu Thr Arg Arg Asn Ile Val Gly Cys Arg Ile Gln His
      35      40      45
Gly Trp Lys Glu Gly Asn Glu Pro Val Glu Gln Trp Lys Gly Thr Val
      50      55      60
Leu Asp Pro Gly Ile Arg
      65      70

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<210> 346  
 <211> 255  
 <212> PRT  
 <213> Homo sapiens

```

    <400> 346
Ala Pro Asp Ser Asp Gly Gly Ser Asp Ala Asp Ser Glu Val Gly Pro
  1      5      10      15
Gly Ser Pro Thr Arg Thr Ala Glu Ala Glu Glu Glu Met Ala Gly
      20      25      30
Pro Asn Gln Leu Cys Ile Arg Arg Trp Thr Thr Lys His Val Ala Val
      35      40      45
Trp Leu Lys Asp Glu Gly Phe Phe Glu Tyr Val Asp Ile Leu Cys Asn
      50      55      60
Lys His Arg Leu Asp Gly Ile Thr Leu Leu Thr Leu Thr Glu Tyr Asp
      65      70      75      80
Leu Arg Ser Pro Pro Leu Glu Ile Lys Val Leu Gly Asp Ile Lys Arg
      85      90      95
Leu Met Leu Ser Val Arg Lys Leu Gln Lys Ile His Ile Asp Val Leu
      100      105      110
Glu Glu Met Gly Tyr Asn Ser Asp Ser Pro Met Gly Ser Met Thr Pro
      115      120      125
Phe Ile Ser Ala Leu Gln Ser Thr Asp Trp Leu Cys Asn Gly Glu Leu
      130      135      140
Ser His Asp Cys Asp Gly Pro Ile Thr Asp Leu Asn Ser Asp Gln Tyr
      145      150      155      160
Gln Tyr Met Asn Gly Lys Asn Lys His Ser Val Arg Arg Leu Asp Pro
      165      170      175

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PCT/US00/34960

Glu Tyr Trp Lys Thr Ile Leu Ser Cys Ile Tyr Val Phe Ile Val Phe  
                   180                  185                  190  
 Gly Phe Thr Ser Phe Ile Met Val Ile Val His Glu Arg Val Pro Asp  
                   195                  200                  205  
 Met Gln Thr Tyr Pro Pro Leu Pro Asp Ile Phe Leu Asp Ser Val Pro  
                   210                  215                  220  
 Arg Ile Pro Trp Ala Phe Ala Met Thr Glu Val Cys Gly Met Ile Leu  
                   225                  230                  235                  240  
 Cys Tyr Ile Trp Leu Leu Val Leu Leu Leu His Lys His Arg Ser  
                   245                  250                  255

<210> 347  
 <211> 313  
 <212> PRT  
 <213> Homo sapiens

<400> 347  
 Lys Thr Cys Phe Glu Lys Ala Leu Glu Gly Asn Pro Glu Asn Pro Glu  
   1                  5                  10                  15  
 Phe Asn Thr Gly Tyr Ala Ile Thr Val Tyr Arg Leu Asp Lys Phe Asn  
                   20                  25                  30  
 Thr Ala Ser Gly Arg Asn Lys Ala Phe Ser Leu His Val Leu Lys Arg  
                   35                  40                  45  
 Ala Val Arg Leu Asn Pro Asp Asp Val Tyr Ile Arg Val Leu Leu Ala  
                   50                  55                  60  
 Leu Lys Leu Gln Asp Glu Gly Gln Glu Ala Glu Gly Glu Lys Tyr Ile  
                   65                  70                  75                  80  
 Glu Glu Ala Leu Thr Ser Ile Ser Ser Gln Ala Tyr Val Phe Gln Tyr  
                   85                  90                  95  
 Ala Ala Lys Phe Tyr Arg Arg Lys Gly Ser Val Asp Lys Ala Leu Glu  
                   100                  105                  110  
 Leu Leu Lys Met Ala Leu Glu Thr Thr Pro Thr Ser Ala Phe Leu His  
                   115                  120                  125  
 His Gln Met Gly Leu Cys Tyr Arg Ala Gln Met Ile Gln Ile Lys Glu  
                   130                  135                  140  
 Ala Thr Asn Trp Gln Pro Arg Gly Gln Asp Arg Glu Thr Val Asp Arg  
                   145                  150                  155                  160  
 Leu Val Gln Leu Ala Ile Cys Lys Phe Glu Lys Thr Ile Met Leu Lys  
                   165                  170                  175  
 Arg Thr Phe Glu Met Ala Tyr Val Asp Leu Ala Glu Thr Tyr Ala Glu  
                   180                  185                  190  
 Ile Gly His His Arg Lys Ala Glu His Phe Gln Lys Gly Leu Arg  
                   195                  200                  205  
 Met Lys Ile Phe Glu Asp Gln Leu Lys Gln Glu Ile His Tyr His Tyr  
                   210                  215                  220  
 Gly Arg Phe Gln Glu His His Gly Lys Ser Gln Asp Lys Ala Ile Thr  
                   225                  230                  235                  240  
 His Tyr Leu Lys Gly Leu Lys Ile Glu Lys Met Ser His Ser Arg Glu  
                   245                  250                  255  
 Lys Leu Leu Asn Ala Leu Glu Lys Leu Ala Lys Arg Cys Ile His Gln  
                   260                  265                  270  
 Asn Val Arg Val Val Glu Ser Val Ser Leu Leu Gly Leu Ile His Lys  
                   275                  280                  285  
 Leu Lys Gly Glu Val Ser Asp Ala Leu Leu Cys Tyr Glu Arg Ala Leu  
                   290                  295                  300  
 Arg Leu Ala Ala Asp Leu Asn Pro  
                   305                  310                  312

<210> 348  
 <211> 227

<212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(227)  
 <223> Xaa = any amino acid or nothing

<400> 348  
 Ser Thr Asp Leu Ser Gln Thr Glu Leu Arg Asp Gly Gln Leu Lys Arg  
 1 5 10 15  
 Arg Asn Met Glu Glu Asn Ile Asn Cys Phe Ser His Thr Asn Val Gln  
 20 25 30  
 Pro Cys Val Ile Thr Thr Asp Asn Ala Leu Cys Arg Glu Gly Pro Met  
 35 40 45  
 Thr Gly Ser Val Met Asn Leu Val Ser Asn Asn Ser Ile Glu Asp Ser  
 50 55 60  
 Asp Met Asp Ser Asp Asp Glu Ile Leu Thr Leu Cys Thr Ser Ser Arg  
 65 70 75 80  
 Lys Arg Asn Lys Pro Lys Trp Asp Leu Asp Asp Glu Ile Leu Gln Leu  
 85 90 95  
 Glu Thr Pro Pro Lys Tyr His Thr Gln Ile Asp Tyr Val His Cys Leu  
 100 105 110  
 Val Pro Asp Leu Leu Gln Ile Asn Asn Asn Pro Cys Tyr Trp Gly Val  
 115 120 125  
 Met Asp Lys Tyr Ala Ala Glu Ala Leu Leu Glu Gly Lys Pro Glu Gly  
 130 135 140  
 Thr Phe Leu Leu Arg Asp Ser Ala Gln Glu Asp Tyr Leu Phe Ser Val  
 145 150 155 160  
 Ser Phe Arg Arg Tyr Ser Arg Ser Leu His Ala Arg Ile Glu Gln Trp  
 165 170 175  
 Asn His Asn Phe Ser Phe Asp Ala His Asp Pro Xaa Val Phe His Ser  
 180 185 190  
 Pro Asp Ile Thr Gly Leu Leu Glu His Tyr Lys Asp Pro Ser Ala Cys  
 195 200 205  
 Met Phe Phe Glu Pro Leu Leu Ser Thr Pro Leu Ile Arg Thr Phe Pro  
 210 215 220  
 Phe Cys Leu  
 225 227

<210> 349  
 <211> 146  
 <212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(146)  
 <223> Xaa = any amino acid or nothing

<400> 349.  
 Gly Arg Pro Thr Arg Pro Lys Asn Lys Glu Asn Gly Lys Val Glu Asn  
 1 5 10 15  
 Gly Leu Gly Lys Thr Asp Arg Lys Lys Glu Ile Val Lys Phe Glu Pro  
 20 25 30  
 Gln Val Asp Thr Glu Ala Glu Asp Met Ile Ser Ala Val Lys Ser Lys  
 35 40 45  
 Arg Leu Leu Ala Ile Gln Ala Lys Lys Glu Arg Glu Ile Gln Glu Arg  
 50 55 60  
 Glu Met Lys Gly Lys Ile Ser Cys Xaa Glu Lys Gly Glu Ala Leu Xaa  
 65 70 75 80  
 Lys Asn Lys Glu Asn Gly Lys Val Glu Asn Gly Leu Gly Lys Thr Asp

```

      85      90      95
Arg Lys Lys Glu Ile Val Lys Phe Glu Pro Gln Val Asp Thr Glu Ala
      100      105      110
Glu Asp Met Ile Ser Ala Val Lys Ser Lys Arg Leu Leu Ala Ile Gln
      115      120      125
Ala Lys Lys Glu Arg Glu Ile Gln Glu Arg Glu Met Lys Gly Lys Ile
      130      135      140
Ser Cys
145 146

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<210> 350
<211> 69
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(69)
<223> Xaa = any amino acid or nothing

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<400> 350
Lys Tyr Arg Gly Tyr Leu Tyr Phe Ala Ala Leu Leu Phe Arg Phe Phe
 1      5      10      15
Pro Lys Cys Ala Leu Tyr Val Asp Cys Ile Phe Ser Phe Ser Phe Gln
      20      25      30
Val Lys Val Val Glu Lys Tyr Phe Ser Gly Pro Ala Ile Thr Leu Glu
      35      40      45
Asn Thr Arg Val Val Ser Gln Ser Leu Gln His Tyr Leu Xaa Leu Gly
      50      55      60
Arg Val Ser Val Gln
65      69

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<210> 351
<211> 243
<212> PRT
<213> Homo sapiens

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<400> 351
Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Val
 1      5      10      15
Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala
      20      25      30
His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser
      35      40      45
Pro Ala Thr Ala His Leu Pro Val Pro Ser Pro Ala Thr Ala His Leu
      50      55      60
Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala
65      70      75      80
Thr Ala His Leu Pro Val Pro Ser Pro Ala Thr Ala His Leu Pro Ala
      85      90      95
Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala
      100      105      110
His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Val Pro Ser
      115      120      125
Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu
      130      135      140
Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Val Pro Ser Pro Ala
145      150      155      160
Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu Pro Ala
      165      170      175

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Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala
      180      185      190
His Leu Pro Val Pro Ser Pro Ala Thr Ala His Leu Pro Ala Pro Ser
      195      200      205
Pro Ala Thr Ala His Leu Pro Ala Pro Ser Pro Ala Thr Ala His Leu
      210      215      220
Pro Val Leu Thr Cys His Gly Pro Pro Phe His Pro His Leu Pro Gln
      225      230      235      240
Leu Thr Leu
      243

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<210> 352
<211> 107
<212> PRT
<213> Homo sapiens

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<400> 352
Gln Ile Leu Gly Lys Val Tyr Ser Val Leu Ser Asp Arg Glu Gln Arg
  1           5           10           15
Ala Val Tyr Asp Glu Gln Gly Thr Val Asp Glu Asp Ser Pro Val Leu
      20      25      30
Thr Gln Asp Arg Asp Trp Glu Ala Tyr Trp Arg Leu Leu Phe Lys Lys
      35      40      45
Ile Ser Leu Glu Asp Ile Gln Ala Phe Glu Lys Thr Tyr Lys Gly Ser
      50      55      60
Glu Glu Glu Leu Ala Asp Ile Lys Gln Ala Tyr Leu Asp Phe Lys Gly
      65      70      75      80
Asp Met Asp Gln Ile Met Glu Ser Val Leu Cys Val Gln Tyr Thr Glu
      85      90      95
Glu Pro Arg Ile Arg Asn Ile Ile Gln Gln Ala
      100      105      107

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<210> 353
<211> 199
<212> PRT
<213> Homo sapiens

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```

<400> 353
Leu Ser Arg Asn Leu Asp Val Arg Ala Phe Ile Tyr Lys Thr Leu Met
  1           5           10           15
Pro Ser Glu Ala Asn Gly Leu Leu Asn Ser Leu Leu Asp Ile Val Ser
      20      25      30
Ser Leu Ser Ala Leu Leu Ala Lys Ala Gln His Val Phe Glu Tyr Leu
      35      40      45
Pro Glu Phe Leu His Thr Phe Lys Ile Thr Ala Leu Leu Glu Thr Leu
      50      55      60
Asp Phe Gln Gln Val Ser Gln Asn Val Gln Ala Arg Ser Ser Ala Phe
      65      70      75      80
Gly Ser Phe Gln Phe Val Met Lys Met Val Cys Lys Asp Gln Ala Ser
      85      90      95
Phe Leu Ser Asp Ser Asn Met Phe Ile Asn Leu Pro Arg Val Lys Glu
      100      105      110
Leu Leu Glu Asp Asp Lys Glu Lys Phe Asn Ile Pro Glu Asp Ser Thr
      115      120      125
Pro Phe Cys Leu Lys Leu Tyr Gln Glu Ile Leu Gln Leu Pro Asn Gly
      130      135      140
Ala Leu Val Trp Thr Phe Leu Lys Pro Ile Leu His Gly Lys Ile Leu
      145      150      155      160
Tyr Thr Pro Asn Thr Pro Glu Ile Asn Lys Val Ile Gln Lys Ala Asn

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165 170 175  
 Tyr Thr Phe Tyr Ile Val Asp Lys Leu Lys Thr Leu Ser Glu Thr Leu  
 180 185 190  
 Leu Glu Met Ser Ser Leu Phe  
 195 199

<210> 354  
 <211> 87  
 <212> PRT  
 <213> Homo sapiens

<400> 354  
 Thr Ile Gly Arg Gln Tyr Leu Leu Lys Lys Lys Thr Gly Thr Ile Val  
 1 5 10 15  
 Glu Glu Arg Val Asn Arg Pro Gly Trp Asn Glu Asp Asp Val Ser  
 20 25 30  
 Val Ser Asp Glu Ser Glu Leu Pro Thr Ser Thr Thr Leu Lys Ala Ser  
 35 40 45  
 Glu Lys Ser Thr Met Glu Gln Leu Val Glu Lys Ala Cys Phe Arg Asp  
 50 55 60  
 Tyr Gln Arg Leu Gly Leu Gly Thr Ile Ser Gly Ser Ser Arg Ser  
 65 70 75 80  
 Arg Pro Glu Ser Arg Arg Gly  
 85 87

<210> 355  
 <211> 231  
 <212> PRT  
 <213> Homo sapiens

<400> 355  
 Thr Leu Glu Phe Glu Lys Glu Asp Leu Met Asn Gly Val Lys Lys Glu  
 1 5 10 15  
 Ile Ser Ile Ser Ile Ile Gly Lys Lys Arg Lys Arg Cys Val Val Phe  
 20 25 30  
 Asn Gln Gly Glu Leu Asp Ala Met Glu Tyr His Thr Lys Ile Arg Glu  
 35 40 45  
 Leu Ile Leu Asp Gly Ser Leu Gln Leu Ile Gln Glu Gly Leu Lys Ser  
 50 55 60  
 Gly Phe Leu Tyr Pro Leu Phe Glu Lys Gln Asp Lys Gly Ser Lys Pro  
 65 70 75 80  
 Ile Thr Leu Pro Leu Asp Ala Cys Ser Leu Ser Glu Leu Cys Glu Met  
 85 90 95  
 Ala Lys His Leu Pro Ser Leu Asn Glu Met Glu His Gln Thr Leu Gln  
 100 105 110  
 Leu Val Glu Glu Asp Thr Ser Val Thr Glu Gln Asp Leu Phe Leu Arg  
 115 120 125  
 Val Val Glu Asn Asn Ser Ser Phe Thr Lys Val Ile Thr Leu Met Gly  
 130 135 140  
 Gln Lys Tyr Leu Leu Pro Pro Lys Ser Ser Phe Leu Leu Ser Asp Ile  
 145 150 155 160  
 Ser Cys Met Gln Pro Leu Leu Asn Tyr Arg Lys Thr Phe Asp Val Ile  
 165 170 175  
 Val Ile Asp Pro Trp Gln Asn Lys Ser Val Lys Arg Ser Asn Arg  
 180 185 190  
 Tyr Ser Tyr Leu Ser Pro Leu Gln Ile Lys Gln Ile Pro Ile Pro Lys  
 195 200 205  
 Leu Ala Ala Pro Asn Cys Leu Leu Val Thr Trp Val Thr Asn Arg Gln  
 210 215 220

Lys His Leu Arg Phe Ile Lys  
225 230 231

<210> 356  
<211> 262  
<212> PRT  
<213> Homo sapiens

<400> 356  
Asp Ala Trp Ala Asp Ala Trp Asp Arg Phe Val Ala Asp Phe Lys Ala  
1 5 10 15  
Gln Gly Pro Pro Lys Pro Asn Thr Asp Glu Gly Gly Ala Val Leu Pro  
20 25 30  
Ser Cys Ala Asp Leu Phe Val Tyr Tyr Lys Lys Cys Met Val Gln Cys  
35 40 45  
Ser Gln Leu Ser Thr Gly Glu Pro Met Ile Ala Leu Thr Thr Ile Phe  
50 55 60  
Gln Lys Tyr Leu Arg Glu Tyr Ala Trp Lys Ile Leu Ser Gly Asn Leu  
65 70 75 80  
Pro Lys Thr Thr Thr Ser Ser Gly Gly Leu Thr Ile Ser Ser Leu Leu  
85 90 95  
Lys Glu Lys Glu Gly Ser Glu Val Ala Lys Phe Thr Leu Glu Glu Leu  
100 105 110  
Cys Leu Ile Cys Asn Ile Leu Ser Thr Ala Glu Tyr Cys Leu Ala Thr  
115 120 125  
Thr Gln Gln Leu Glu Glu Lys Leu Lys Glu Lys Val Asp Val Ser Leu  
130 135 140  
Ile Glu Arg Ile Asn Leu Thr Gly Glu Met Asp Thr Phe Ser Thr Val  
145 150 155 160  
Ile Ser Ser Ser Ile Gln Leu Leu Val Gln Asp Leu Asp Ala Ala Cys  
165 170 175  
Asp Pro Ala Leu Thr Ala Met Ser Lys Met Gln Trp Gln Asn Val Glu  
180 185 190  
His Val Gly Asp Gln Ser Pro Tyr Val Thr Ser Val Ile Leu His Ile  
195 200 205  
Lys Gln Asn Val Pro Ile Ile Arg Asp Asn Leu Ala Ser Thr Arg Lys  
210 215 220  
Tyr Phe Thr Gln Phe Cys Val Lys Phe Ala Asn Ser Phe Ile Pro Lys  
225 230 235 240  
Phe Ile Thr His Leu Phe Lys Cys Lys Pro Ile Ser Met Val Gly Ala  
245 250 255  
Glu Gln Val Arg Trp Thr  
260 262

<210> 357  
<211> 199  
<212> PRT  
<213> Homo sapiens

<400> 357  
Pro Arg Cys Arg Asn Ser Ala Arg Val Ala Asp Thr Phe Tyr Thr Asn  
1 5 10 15  
Ala Gly Cys Thr Leu Val Ala Leu Asn Pro Phe Lys Pro Val Pro Gln  
20 25 30  
Leu Tyr Ser Pro Glu Leu Met Arg Glu Tyr His Ala Ala Pro Gln Pro  
35 40 45  
Gln Lys Leu Lys Pro His Val Phe Thr Val Gly Glu Gln Thr Tyr Arg  
50 55 60  
Asn Val Lys Ser Leu Ile Glu Pro Val Asn Gln Ser Ile Val Val Ser

```

65              70              75              80
Gly Glu Ser Gly Ala Gly Lys Thr Trp Thr Ser Arg Cys Leu Met Lys
      85              90              95
Phe Tyr Ala Val Val Ala Thr Ser Pro Ala Ser Trp Glu Ser His Lys
      100              105              110
Ile Ala Glu Arg Ile Glu Gln Arg Ile Leu Asn Ser Asn Pro Val Met
      115              120              125
Glu Ala Phe Gly Asn Ala Cys Thr Leu Arg Asn Asn Asn Ser Ser Arg
      130              135              140
Phe Gly Lys Phe Ile Gln Leu Gln Leu Asn Arg Ala Gln Gln Met Thr
145              150              155              160
Gly Ala Ala Val Gln Thr Tyr Leu Leu Glu Lys Thr Arg Val Ala Cys
      165              170              175
Gln Ala Ser Ser Glu Arg Asn Lys Asp Pro Ile Pro Pro Glu Leu Thr
      180              185              190
Arg Leu Leu Gln Gln Ser Gln
      195              199

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<210> 358
<211> 252
<212> PRT
<213> Homo sapiens

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```

<400> 358
His Glu Asp Met Ser Ser Pro Gly Leu Glu Leu Pro Ser Cys Glu Leu
 1              5              10              15
Ser Arg Leu Glu Glu Ile Ala Glu Leu Val Ala Ser Ser Leu Pro Ser
      20              25              30
Pro Leu Arg Arg Glu Lys Leu Ala Leu Ala Leu Glu Asn Glu Gly Tyr
      35              40              45
Ile Lys Lys Leu Leu Glu Leu Phe His Val Cys Glu Asp Leu Glu Asn
      50              55              60
Ile Glu Gly Leu His His Leu Tyr Glu Ile Ile Lys Gly Ile Phe Leu
      65              70              75              80
Leu Asn Arg Thr Ala Leu Phe Glu Val Met Phe Ser Glu Glu Cys Ile
      85              90              95
Met Asp Val Ile Gly Cys Leu Glu Tyr Asp Pro Ala Leu Ser Gln Pro
      100              105              110
Arg Lys His Arg Glu Phe Leu Thr Lys Thr Ala Lys Phe Lys Glu Val
      115              120              125
Ile Pro Ile Ser Asp Pro Glu Leu Lys Gln Lys Ile His Gln Thr Tyr
      130              135              140
Arg Val Gln Tyr Ile Gln Asp Met Val Leu Pro Thr Pro Ser Val Phe
145              150              155              160
Glu Glu Asn Met Leu Ser Thr Leu His Ser Phe Ile Phe Phe Asn Lys
      165              170              175
Val Glu Ile Val Gly Met Leu Gln Glu Asp Glu Lys Phe Leu Thr Asp
      180              185              190
Leu Phe Ala Gln Leu Thr Asp Glu Ala Thr Asp Glu Glu Lys Arg Gln
      195              200              205
Glu Leu Val Asn Phe Leu Lys Glu Phe Cys Ala Phe Ser Gln Thr Leu
      210              215              220
Gln Pro Gln Asn Arg Asp Ala Phe Phe Lys Thr Leu Ser Asn Met Gly
225              230              235              240
Ile Leu Pro Ala Leu Glu Val Ile Leu Gly Met Asp
      245              250              252

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```

<210> 359
<211> 132
<212> PRT

```

&lt;213&gt; Homo sapiens

&lt;400&gt; 359

```

Asn Asp Pro Val Arg Ser Lys Phe Cys Lys Ile Arg Val Leu Cys His
 1          5          10          15
Thr Leu Ala Arg Asn Met Val Tyr Ile Leu Thr Ile Thr Thr Pro Leu
          20          25          30
Lys Ser Ser Asp Ser Arg Lys Arg Lys Ala Val Ile Leu Thr Ala Arg
          35          40          45
Val His Pro Gly Glu Thr Asn Ser Ser Trp Ile Met Lys Gly Phe Leu
          50          55          60
Asp Tyr Ile Leu Gly Asn Ser Ser Asp Ala Gln Leu Leu Arg Asp Thr
          65          70          75          80
Phe Val Phe Lys Val Val Pro Met Leu Asn Pro Asp Gly Val Ile Val
          85          90          95
Gly Asn Tyr Arg Cys Ser Leu Ala Gly Arg Asp Leu Asn Arg Asn Tyr
          100          105          110
Thr Ser Leu Leu Lys Glu Ser Phe Pro Ser Val Trp Tyr Thr Arg Asn
          115          120          125
Met Val His Arg
          130          132

```

&lt;210&gt; 360

&lt;211&gt; 270

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 360

```

Gln Glu Ala Thr Gly Leu Gly Thr Ser Thr Gln Pro Leu Thr Ser Ser
 1          5          10          15
Ala Ser Ser Leu Thr Gly Phe Ser Asn Trp Ser Ala Ala Ile Ala Pro
          20          25          30
Ser Ser Ser Thr Ile Ile Asn Glu Asp Ala Ser Phe Phe His Gln Gly
          35          40          45
Gly Val Pro Ala Ala Ser Ala Asn Asn Gly Ala Leu Leu Phe Gln Asn
          50          55          60
Phe Pro His His Val Ser Pro Gly Phe Gly Gly Ser Phe Ser Pro Gln
          65          70          75          80
Ile Gly Pro Leu Ser Gln His His Pro His His Pro His Phe Gln His
          85          90          95
His His Ser Gln His Gln Gln Arg Arg Ser Pro Ala Ser Pro His
          100          105          110
Pro Pro Pro Phe Thr His Arg Asn Ala Ala Phe Asn Gln Leu Pro His
          115          120          125
Leu Ala Asn Asn Leu Asn Lys Pro Pro Ser Pro Trp Ser Ser Tyr Gln
          130          135          140
Ser Pro Ser Pro Thr Pro Ser Ser Ser Trp Ser Pro Gly Gly Gly Gly
          145          150          155          160
Tyr Gly Gly Trp Gly Gly Ser Gln Gly Arg Asp His Arg Arg Gly Leu
          165          170          175
Asn Gly Gly Ile Thr Pro Leu Asn Ser Ile Ser Pro Leu Lys Lys Asn
          180          185          190
Phe Ala Ser Asn His Ile Gln Leu Gln Lys Tyr Ala Arg Pro Ser Ser
          195          200          205
Ala Phe Ala Pro Lys Ser Trp Met Glu Asp Ser Leu Asn Arg Ala Asp
          210          215          220
Asn Ile Phe Pro Phe Pro Asp Arg Pro Arg Thr Phe Asp Met His Ser
          225          230          235          240
Leu Glu Ser Ser Leu Ile Asp Ile Met Arg Ala Glu Asn Asp Thr Ile
          245          250          255

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Lys Gly Gln Ser Ser Leu Phe Pro Met Glu Asp Gly Phe Leu  
                   260                                  265                                  270

<210> 361  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<400> 361  
 Glu Arg Gly Gly Ala Gln Val Asn Ala Thr Asp Glu Ile Lys Arg Glu  
   1                                  5                                  10                                  15  
 Ile Ile His Gln Leu Ser Ile Lys Pro Met Ala His Ser Glu Leu Val  
                                   20                                  25                                  30  
 Lys Ser Leu Pro Glu Asp Val Ser Thr Tyr Ile Ser Lys Lys Lys Thr  
                                   35                                  40                                  45  
 Ile Glu Thr Phe Pro Cys Leu Ser Val  
                   50                                  55                                  57

<210> 362  
 <211> 377  
 <212> PRT  
 <213> Homo sapiens

<400> 362  
 Ser Glu Phe Lys Met Leu Lys Arg Lys Pro Ser Asn Val Ser Glu Lys  
   1                                  5                                  10                                  15  
 Glu Lys His Gln Lys Pro Lys Arg Ser Ser Ser Phe Gly Asn Phe Asp  
                                   20                                  25                                  30  
 Arg Phe Arg Asn Asn Ser Leu Ser Lys Pro Asp Asp Ser Thr Glu Ala  
                                   35                                  40                                  45  
 His Glu Gly Asp Pro Thr Asn Gly Ser Gly Glu Gln Ser Lys Thr Ser  
                                   50                                  55                                  60  
 Asn Asn Gly Gly Gly Leu Gly Lys Lys Met Arg Ala Ile Ser Trp Thr  
   65                                  70                                  75                                  80  
 Met Lys Lys Lys Val Gly Lys Lys Tyr Ile Lys Ala Leu Ser Glu Glu  
                                   85                                  90                                  95  
 Lys Asp Glu Glu Asp Gly Glu Asn Ala His Pro Tyr Arg Asn Ser Asp  
                                   100                                  105                                  110  
 Pro Val Ile Gly Thr His Thr Glu Lys Val Ser Leu Lys Ala Ser Asp  
                                   115                                  120                                  125  
 Ser Met Asp Ser Leu Tyr Ser Gly Gln Ser Ser Ser Ser Gly Ile Thr  
                                   130                                  135                                  140  
 Ser Cys Ser Asp Gly Thr Ser Asn Arg Asp Ser Phe Arg Leu Asp Asp  
  145                                  150                                  155                                  160  
 Asp Gly Pro Tyr Ser Gly Pro Phe Cys Gly Arg Ala Arg Val His Thr  
                                   165                                  170                                  175  
 Asp Phe Thr Pro Ser Pro Tyr Asp Thr Asp Ser Leu Lys Ile Lys Lys  
                                   180                                  185                                  190  
 Gly Asp Ile Ile Asp Ile Ile Cys Lys Thr Pro Met Gly Met Trp Thr  
                                   195                                  200                                  205  
 Gly Met Leu Asn Asn Lys Val Gly Asn Phe Lys Phe Ile Tyr Val Asp  
  210                                  215                                  220  
 Val Ile Ser Glu Glu Glu Ala Ala Pro Lys Lys Ile Lys Ala Asn Arg  
  225                                  230                                  235                                  240  
 Arg Ser Asn Ser Lys Lys Ser Lys Thr Leu Gln Glu Phe Leu Glu Arg  
                                   245                                  250                                  255  
 Ile His Leu Gln Glu Tyr Thr Ser Thr Leu Leu Leu Asn Gly Tyr Glu  
                                   260                                  265                                  270  
 Thr Leu Glu Asp Leu Lys Asp Ile Lys Glu Ser His Leu Ile Glu Leu

275 280 285  
 Asn Ile Glu Asn Pro Asp Asp Arg Arg Arg Leu Leu Ser Ala Ala Glu  
 290 295 300  
 Asn Phe Leu Glu Glu Glu Ile Ile Gln Glu Gln Glu Asn Glu Pro Glu  
 305 310 315 320  
 Pro Leu Ser Leu Ser Ser Asp Ile Ser Leu Asn Lys Ser Gln Leu Asp  
 325 330 335  
 Asp Cys Pro Arg Asp Ser Gly Cys Tyr Ile Ser Ser Gly Asn Ser Asp  
 340 345 350  
 Asn Gly Lys Glu Asp Leu Glu Ser Glu Asn Leu Ser Asp Met Val His  
 355 360 365  
 Lys Ile Ile Ile Thr Glu Pro Ser Asp  
 370 375 377

<210> 363  
 <211> 95  
 <212> PRT  
 <213> Homo sapiens

<400> 363  
 Pro Ala Gly Arg Cys Pro Val Ser Lys Gly Gly Gly Ala Gly Leu Gln  
 1 5 10 15  
 Ala His Asn Pro Ala Lys Lys Thr Arg Thr Thr Leu Leu Asn Glu Thr  
 20 25 30  
 Gln Ile Phe Ser Tyr Phe Ser Gln Phe Gly Thr Val Thr Gln Phe Arg  
 35 40 45  
 Leu Ser Arg Ser Lys Met Thr Gly Asn Gly Lys Gly Tyr Ala Phe Val  
 50 55 60  
 Glu Phe Glu Ser Glu Asp Val Ala Lys Ile Val Ala Glu Thr Met Asn  
 65 70 75 80  
 Asn Tyr Leu Phe Gly Glu Arg Leu Leu Glu Cys His Gly Arg Val  
 85 90 95

<210> 364  
 <211> 190  
 <212> PRT  
 <213> Homo sapiens

<400> 364  
 Ser Tyr Leu Gly Asp Gln Ser Gly Glu Lys Leu Phe Asp Cys Ser Gln  
 1 5 10 15  
 Cys Arg Lys Ser Phe His Cys Lys Ser Tyr Val Leu Glu His Gln Arg  
 20 25 30  
 Ile His Thr Gln Glu Lys Pro Tyr Lys Cys Thr Lys Cys Arg Lys Thr  
 35 40 45  
 Phe Arg Trp Arg Ser Asn Phe Thr Arg His Met Arg Leu His Glu Glu  
 50 55 60  
 Glu Lys Phe Tyr Lys Gln Asp Glu Cys Arg Glu Gly Phe Arg Gln Ser  
 65 70 75 80  
 Pro Asp Cys Ser Gln Pro Gln Gly Ala Pro Ala Val Glu Lys Thr Phe  
 85 90 95  
 Leu Cys Gln Gln Cys Gly Lys Thr Phe Thr Arg Lys Lys Thr Leu Val  
 100 105 110  
 Asp His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Gln Cys Ser Asp  
 115 120 125  
 Cys Gly Lys Asp Phe Ala Tyr Arg Ser Ala Phe Ile Val His Lys Lys  
 130 135 140  
 Lys His Ala Met Lys Arg Lys Pro Glu Gly Gly Pro Ser Phe Gln Ser  
 145 150 155 160

Gly His Ser Val Pro Gly Ser Ser Asn Ser His Ser Lys Lys Glu Pro  
                   165                  170                  175  
 Tyr Lys Cys Ser Gln Cys Gly Lys Ala Phe Arg Asn His Ser  
                   180                  185                  190

<210> 365  
 <211> 201  
 <212> PRT  
 <213> Homo sapiens

<400> 365  
 Ser Cys Asn Trp Phe Gly Lys Gly Lys Arg Gly Phe Ile Met Gly Ile  
   1                  5                  10                  15  
 Trp Asn Ser His Thr Ser Val Gly Asp Ile Leu Gly Ser Leu Ile Ala  
                   20                  25                  30  
 Gly Ile Trp Val Asn Gly Gln Trp Gly Leu Ser Phe Ile Val Pro Gly  
                   35                  40                  45  
 Ile Ile Thr Ala Val Met Gly Val Ile Thr Phe Leu Phe Leu Ile Glu  
                   50                  55                  60  
 His Pro Glu Asp Val Asp Cys Ala Pro Pro Gln His His Gly Glu Pro  
                   65                  70                  75                  80  
 Ala Glu Asn Gln Asp Asn Pro Glu Asp Pro Gly Asn Ser Pro Cys Ser  
                   85                  90                  95  
 Ile Lys Glu Ser Gly Leu Glu Thr Val Ala Lys Cys Ser Lys Gly Pro  
                   100                  105                  110  
 Cys Glu Glu Pro Ala Ala Ile Ser Phe Phe Gly Ala Leu Arg Ile Pro  
                   115                  120                  125  
 Gly Val Asp Glu Phe Ser Leu Cys Leu Leu Ile Ala Lys Leu Val Ser  
                   130                  135                  140  
 Tyr Thr Phe Leu Tyr Trp Leu Pro Leu Tyr Ile Ala Asn Val Ala His  
                   145                  150                  155                  160  
 Phe Ser Ala Lys Glu Ala Gly Asp Leu Ser Thr Leu Phe His Val Gly  
                   165                  170                  175  
 Gly Ile Ile Gly Gly Ile Glu Ala Gly Leu Val Ser Asp Tyr Thr Asn  
                   180                  185                  190  
 Gly Arg Ala Thr Thr Cys Cys Val Met  
                   195                  200 201

<210> 366  
 <211> 212  
 <212> PRT  
 <213> Homo sapiens

<400> 366  
 Leu Gly Lys Glu Arg Lys His Leu His Gln Thr Lys Phe Ala Asp Asp  
   1                  5                  10                  15  
 Phe Arg Lys Arg His Pro Asn Val His Phe Val Leu Asn Gln Glu Ser  
                   20                  25                  30  
 Met Thr Leu Thr Gly Leu Pro Asn His Leu Ala Lys Ala Lys Gln Tyr  
                   35                  40                  45  
 Val Leu Lys Gly Gly Gly Met Ser Leu Ala Gly Lys Lys Leu Lys  
                   50                  55                  60  
 Glu Gly His Glu Thr Pro Met Asp Ile Asp Ser Asp Asp Ser Lys Ala  
                   65                  70                  75                  80  
 Ala Ser Pro Pro Leu Lys Gly Ser Val Ser Ser Glu Ala Ser Glu Leu  
                   85                  90                  95  
 Asp Lys Lys Glu Lys Gly Ile Cys Val Ile Cys Met Asp Thr Ile Ser  
                   100                  105                  110  
 Asn Lys Lys Val Leu Pro Lys Cys Lys His Glu Phe Cys Ala Pro Cys



```

      115      120      125
Ile Asn Lys Ala Met Ser Tyr Lys Pro Ile Cys Pro Thr Cys Gln Thr
      130      135      140
Ser Tyr Gly Ile Gln Lys Gly Asn Gln Pro Glu Gly Ser Met Val Phe
145      150      155      160
Thr Val Ser Arg Asp Ser Leu Pro Gly Tyr Glu Ser Phe Gly Thr Ile
      165      170      175
Val Ile Thr Tyr Ser Met Lys Ala Gly Ile Gln Thr Glu Glu His Pro
      180      185      190
Asn Pro Gly Lys Arg Tyr Pro Gly Ile Gln Arg Thr Ala Tyr Leu Pro
      195      200      205
Asp Asn Lys Glu
210      212

```

&lt;210&gt; 367

&lt;211&gt; 719

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(713)

&lt;223&gt; Xaa = any amino acid or nothing

&lt;400&gt; 367

```

Asn Lys Lys Thr Leu Glu Ala Pro Glu Gly Ile Arg Asp Lys Val Ser
 1      5      10      15
Asp Trp Asp Glu Phe Leu Arg Gln Thr Leu Ile Gly Ala Cys Ser Pro
      20      25      30
Pro Val Pro Leu Leu Glu Gly Leu Arg Asn Gly Arg Asn Pro Leu Asp
      35      40      45
Leu Ile Ala Pro Gly Ser Arg Leu Glu Cys Gln Ala Phe Gln Asp Ser
      50      55      60
Leu Ser Thr Trp Ile Val Thr Val Val Glu Asn Ile Gly Gly Arg Leu
      65      70      75      80
Lys Leu Arg Tyr Glu Gly Leu Glu Ser Ser Asp Asn Tyr Glu His Trp
      85      90      95
Leu Tyr Tyr Leu Asp Pro Phe Leu His His Val Gly Trp Ala Ala Gln
      100      105      110
Gln Gly Tyr Glu Leu Gln Pro Pro Ser Ala Ile Arg His Leu Lys Asn
      115      120      125
Glu Ala Glu Trp Gln Glu Ile Leu Ala Lys Val Lys Glu Glu Glu Glu
      130      135      140
Glu Pro Leu Pro Ser Tyr Leu Phe Lys Asp Lys Gln Val Ile Gly Ile
145      150      155      160
His Thr Phe Ser Val Asn Met Lys Leu Glu Ala Val Asp Pro Trp Ser
      165      170      175
Pro Phe Gly Ile Ser Pro Ala Thr Val Val Lys Val Phe Asp Glu Lys
      180      185      190
Tyr Phe Leu Val Glu Met Asp Asp Leu Arg Pro Glu Asn His Ala Arg
      195      200      205
Arg Ser Phe Val Cys His Ala Asp Ser Pro Gly Ile Phe Pro Val Gln
      210      215      220
Trp Ser Leu Lys Asn Gly Leu His Ile Ser Pro Pro Pro Gly Tyr Pro
225      230      235      240
Ser Gln Asp Phe Asp Trp Ala Asp Tyr Leu Lys Gln Cys Gly Ala Glu
      245      250      255
Ala Ala Pro Gln Arg Cys Phe Pro Pro Leu Ile Ser Glu His Glu Phe
      260      265      270
Lys Glu Asn Met Lys Leu Glu Ala Val Asn Pro Ile Leu Pro Glu Glu
      275      280      285
Val Cys Val Ala Thr Ile Thr Ala Val Arg Gly Ser Tyr Leu Trp Leu

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      290              295              300
Gln Leu Glu Gly Ser Lys Lys Pro Ile Pro Glu Cys Ile Val Ser Val
305              310              315              320
Glu Ser Met Asp Ile Phe Pro Leu Gly Trp Cys Glu Thr Asn Gly His
      325              330              335
Pro Leu Ser Thr Pro Arg Arg Ala Arg Val Tyr Lys Gln Arg Lys Ile
      340              345              350
Ala Val Val Gln Pro Glu Lys Gln Val Pro Ser Ser Arg Thr Val His
      355              360              365
Glu Gly Leu Arg Asn Gln Glu Leu Asn Ser Thr Glu Ser Val Met Ile
      370              375              380
Asn Gly Lys Tyr Cys Cys Pro Lys Ile Tyr Phe Asn His Arg Cys Phe
385              390              395              400
Ser Gly Pro Tyr Leu Asn Lys Gly Arg Ile Ala Glu Leu Pro Gln Cys
      405              410              415
Val Gly Pro Gly Asn Cys Val Leu Val Leu Arg Glu Val Leu Thr Leu
      420              425              430
Leu Ile Asn Ala Ala Tyr Lys Pro Ser Arg Val Leu Arg Glu Leu Gln
      435              440              445
Leu Asp Lys Asp Ser Val Trp His Gly Cys Gly Glu Val Leu Lys Ala
      450              455              460
Lys Tyr Lys Gly Lys Ser Tyr Arg Ala Thr Val Glu Ile Val Lys Thr
      465              470              475              480
Ala Asp Arg Val Thr Glu Phe Cys Arg Gln Thr Cys Ile Lys Leu Glu
      485              490              495
Cys Cys Pro Asn Leu Phe Gly Pro Arg Met Val Leu Asp Lys Cys Ser
      500              505              510
Glu Asn Cys Ser Val Leu Thr Lys Thr Lys Tyr Thr His Tyr Tyr Gly
      515              520              525
Lys Lys Lys Asn Lys Arg Ile Gly Arg Pro Pro Gly Gly His Ser Asn
      530              535              540
Leu Ala Cys Ala Leu Lys Lys Ala Ser Lys Arg Arg Lys Arg Arg Lys
      545              550              555              560
Asn Val Phe Val His Lys Lys Lys Arg Ser Ser Ala Ser Val Asp Asn
      565              570              575
Thr Pro Ala Gly Phe Phe Pro Arg Gly Ser Gly Gly Xaa Arg Met Arg
      580              585              590
Asp Asp Pro Asp Glu Gly Asp Asp Asp Ser Leu Ser Glu Gly Ser Thr
      595              600              605
Ser Glu Gln Gln Asp Glu Leu Gln Glu Glu Ser Glu Met Ser Glu Lys
      610              615              620
Lys Ser Cys Ser Ser Ser Pro Thr Gln Ser Glu Ile Ser Thr Ser Leu
      625              630              635              640
Pro Pro Asp Arg Gln Arg Arg Lys Arg Glu Leu Arg Thr Phe Ser Phe
      645              650              655
Ser Asp Asp Glu Asn Lys Pro Pro Ser Pro Lys Glu Ile Asp Gly Gln
      660              665              670
Ala Leu Leu Leu Leu Thr Leu Pro Thr Val Gln Glu Cys Met Asp Leu
      675              680              685
Lys Leu Gly Pro Ala Ile Lys Leu Cys His His Ile Glu Arg Ile Lys
      690              695              700
Phe Ala Phe Tyr Glu Gln Phe Ala Asn
705              710              713

```

&lt;210&gt; 368

&lt;211&gt; 719

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(713)

&lt;223&gt; Xaa = any amino acid or nothing

<400> 368

Asn	Lys	Lys	Thr	Leu	Glu	Ala	Pro	Glu	Gly	Ile	Arg	Asp	Lys	Val	Ser
1				5					10					15	
Asp	Trp	Asp	Glu	Phe	Leu	Arg	Gln	Thr	Leu	Ile	Gly	Ala	Cys	Ser	Pro
			20					25					30		
Pro	Val	Pro	Leu	Leu	Glu	Gly	Leu	Arg	Asn	Gly	Arg	Asn	Pro	Leu	Asp
			35				40					45			
Leu	Ile	Ala	Pro	Gly	Ser	Arg	Leu	Glu	Cys	Gln	Ala	Phe	Gln	Asp	Ser
	50					55					60				
Leu	Ser	Thr	Trp	Ile	Val	Thr	Val	Val	Glu	Asn	Ile	Gly	Gly	Arg	Leu
	65			70						75					80
Lys	Leu	Arg	Tyr	Glu	Gly	Leu	Glu	Ser	Ser	Asp	Asn	Tyr	Glu	His	Trp
			85					90						95	
Leu	Tyr	Tyr	Leu	Asp	Pro	Phe	Leu	His	His	Val	Gly	Trp	Ala	Ala	Gln
			100					105					110		
Gln	Gly	Tyr	Glu	Leu	Gln	Pro	Pro	Ser	Ala	Ile	Arg	His	Leu	Lys	Asn
			115			120						125			
Glu	Ala	Glu	Trp	Gln	Glu	Ile	Leu	Ala	Lys	Val	Lys	Glu	Glu	Glu	Glu
	130					135					140				
Glu	Pro	Leu	Pro	Ser	Tyr	Leu	Phe	Lys	Asp	Lys	Gln	Val	Ile	Gly	Ile
	145			150					155					160	
His	Thr	Phe	Ser	Val	Asn	Met	Lys	Leu	Glu	Ala	Val	Asp	Pro	Trp	Ser
			165						170					175	
Pro	Phe	Gly	Ile	Ser	Pro	Ala	Thr	Val	Val	Lys	Val	Phe	Asp	Glu	Lys
			180				185						190		
Tyr	Phe	Leu	Val	Glu	Met	Asp	Asp	Leu	Arg	Pro	Glu	Asn	His	Ala	Arg
			195			200						205			
Arg	Ser	Phe	Val	Cys	His	Ala	Asp	Ser	Pro	Gly	Ile	Phe	Pro	Val	Gln
	210					215					220				
Trp	Ser	Leu	Lys	Asn	Gly	Leu	His	Ile	Ser	Pro	Pro	Pro	Gly	Tyr	Pro
	225			230					235					240	
Ser	Gln	Asp	Phe	Asp	Trp	Ala	Asp	Tyr	Leu	Lys	Gln	Cys	Gly	Ala	Glu
			245					250					255		
Ala	Ala	Pro	Gln	Arg	Cys	Phe	Pro	Pro	Leu	Ile	Ser	Glu	His	Glu	Phe
			260				265						270		
Lys	Glu	Asn	Met	Lys	Leu	Glu	Ala	Val	Asn	Pro	Ile	Leu	Pro	Glu	Glu
			275				280					285			
Val	Cys	Val	Ala	Thr	Ile	Thr	Ala	Val	Arg	Gly	Ser	Tyr	Leu	Trp	Leu
	290					295					300				
Gln	Leu	Glu	Gly	Ser	Lys	Lys	Pro	Ile	Pro	Glu	Cys	Ile	Val	Ser	Val
	305				310					315				320	
Glu	Ser	Met	Asp	Ile	Phe	Pro	Leu	Gly	Trp	Cys	Glu	Thr	Asn	Gly	His
			325					330					335		
Pro	Leu	Ser	Thr	Pro	Arg	Arg	Ala	Arg	Val	Tyr	Lys	Gln	Arg	Lys	Ile
			340				345						350		
Ala	Val	Val	Gln	Pro	Glu	Lys	Gln	Val	Pro	Ser	Ser	Arg	Thr	Val	His
			355				360					365			
Glu	Gly	Leu	Arg	Asn	Gln	Glu	Leu	Asn	Ser	Thr	Glu	Ser	Val	Met	Ile
	370					375					380				
Asn	Gly	Lys	Tyr	Cys	Cys	Pro	Lys	Ile	Tyr	Phe	Asn	His	Arg	Cys	Phe
	385			390						395				400	
Ser	Gly	Pro	Tyr	Leu	Asn	Lys	Gly	Arg	Ile	Ala	Glu	Leu	Pro	Gln	Cys
			405					410					415		
Val	Gly	Pro	Gly	Asn	Cys	Val	Leu	Val	Leu	Arg	Glu	Val	Leu	Thr	Leu
			420				425						430		
Leu	Ile	Asn	Ala	Ala	Tyr	Lys	Pro	Ser	Arg	Val	Leu	Arg	Glu	Leu	Gln
		435				440					445				
Leu	Asp	Lys	Asp	Ser	Val	Trp	His	Gly	Cys	Gly	Glu	Val	Leu	Lys	Ala
	450					455					460				
Lys	Tyr	Lys	Gly	Lys	Ser	Tyr	Arg	Ala	Thr	Val	Glu	Ile	Val	Lys	Thr
	465				470					475					480

Ala Asp Arg Val Thr Glu Phe Cys Arg Gln Thr Cys Ile Lys Leu Glu  
 485 490 495  
 Cys Cys Pro Asn Leu Phe Gly Pro Arg Met Val Leu Asp Lys Cys Ser  
 500 505 510  
 Glu Asn Cys Ser Val Leu Thr Lys Thr Lys Tyr Thr His Tyr Tyr Gly  
 515 520 525  
 Lys Lys Lys Asn Lys Arg Ile Gly Arg Pro Pro Gly Gly His Ser Asn  
 530 535 540  
 Leu Ala Cys Ala Leu Lys Lys Ala Ser Lys Arg Arg Lys Arg Arg Lys  
 545 550 555 560  
 Asn Val Phe Val His Lys Lys Lys Arg Ser Ser Ala Ser Val Asp Asn  
 565 570 575  
 Thr Pro Ala Gly Phe Phe Pro Arg Gly Ser Gly Gly Xaa Arg Met Arg  
 580 585 590  
 Asp Asp Pro Asp Glu Gly Asp Asp Asp Ser Leu Ser Glu Gly Ser Thr  
 595 600 605  
 Ser Glu Gln Gln Asp Glu Leu Gln Glu Glu Ser Glu Met Ser Glu Lys  
 610 615 620  
 Lys Ser Cys Ser Ser Ser Pro Thr Gln Ser Glu Ile Ser Thr Ser Leu  
 625 630 635 640  
 Pro Pro Asp Arg Gln Arg Arg Lys Arg Glu Leu Arg Thr Phe Ser Phe  
 645 650 655  
 Ser Asp Asp Glu Asn Lys Pro Pro Ser Pro Lys Glu Ile Asp Gly Gln  
 660 665 670  
 Ala Leu Leu Leu Leu Thr Leu Pro Thr Val Gln Glu Cys Met Asp Leu  
 675 680 685  
 Lys Leu Gly Pro Ala Ile Lys Leu Cys His His Ile Glu Arg Ile Lys  
 690 695 700  
 Phe Ala Phe Tyr Glu Gln Phe Ala Asn  
 705 710 713

&lt;210&gt; 369

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(426)

&lt;223&gt; Xaa = any amino acid or nothing

&lt;400&gt; 369

Pro Gly Arg Met Val Ser His Thr Pro Ala Pro Pro Ala Ser Phe Pro  
 1 5 10 15  
 Val Pro Tyr Leu Pro Gly Asp Pro Gly Ala Pro Cys Ser Ser Val Leu  
 20 25 30  
 Pro Thr Thr Gly Ile Leu Thr Pro His Pro Gly Pro Gln Asp Ser Trp  
 35 40 45  
 Lys Glu Ala Pro Ala Pro Arg Gly Asn Leu Gln Arg Asn Lys Val Asn  
 50 55 60  
 Ala Ser Phe Pro Thr His Ser Leu Ala His Ser Pro Met Thr Thr Phe  
 65 70 75 80  
 Xaa Phe Leu Gly Gly Phe Ser Gln Ser Phe Pro Phe Ser Asp Cys Pro  
 85 90 95  
 Arg Pro Pro Pro Thr Tyr Ser Ser Phe Leu Arg Thr Leu Phe Phe Leu  
 100 105 110  
 Phe Pro Ser Tyr Thr His Thr Pro Val Ser Ser Leu Pro Ser Phe Pro  
 115 120 125  
 His Ser Leu Phe Cys Leu Leu Val His Cys His Ser Cys His Ser Pro  
 130 135 140  
 Lys Pro Glu Pro Trp Ser Leu Ser Gly Xaa Thr His Val Phe Pro Ser  
 145 150 155 160

```

Val Ser Leu Leu Pro Glu Thr Phe Met Pro Pro Ala Pro Ile Thr Ala
      165      170      175
Pro Val Met Ser Leu Thr Pro Glu Leu Gln Gly Ile Leu Pro Ser Gln
      180      185      190
Pro Pro Val Ser Ser Val Ser His Ala Pro Pro Gly Val Pro Gly Glu
      195      200      205
Leu Ser Leu Gln Val Thr Arg Thr Met Tyr Ser Pro Pro Leu Gly Asn
      210      215      220
Leu Pro Ala Leu Leu Gly Cys Arg Ser Trp Xaa Met Gly Leu Ile Pro
225      230      235      240
Gln Gly Met Cys Xaa Gly Arg Leu Gly Ala Gly Thr Arg Cys Pro Tyr
      245      250      255
Cys Arg Glu Arg Glu Ala Ala His Leu Pro Asn Ser Ala Val Met Gly
      260      265      270
Thr Val Xaa Leu Xaa Val Thr Gly Asp Xaa Ser Leu Gly Lys Pro Xaa
      275      280      285
Glu Gly Gln Leu Ala Pro Leu Ala Phe Leu Pro Ala Ser Leu Ser Ala
290      295      300
Leu Gln His Leu Pro Pro Glu Lys Met Glu Arg Lys Glu Leu Pro Pro
305      310      315      320
Glu His Gln Ser Leu Lys Ser Ser Phe Glu Ala Leu Leu Gln Arg Cys
      325      330      335
Ser Leu Ser Ala Thr Asp Leu Lys Thr Lys Arg Lys Leu Glu Glu Ala
      340      345      350
Ala Gln Arg Leu Glu Tyr Leu Tyr Glu Lys Leu Cys Glu Gly Thr Leu
      355      360      365
Ser Pro His Val Val Ala Gly Leu His Glu Val Ala Arg Cys Val Asp
      370      375      380
Ala Gly Ser Phe Glu Gln Gly Leu Ala Val His Ala Gln Val Ala Gly
385      390      395      400
Cys Ser Ser Phe Ser Glu Val Ser Ser Phe Met Pro Ile Leu Lys Ala
      405      410      415
Val Leu Ile Ile Ala His Lys Leu Leu Val
      420      425 426

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<210> 370
<211> 1074
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(1070)
<223> Xaa = any amino acid or nothing

```

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<400> 370
Thr Glu Ala Asp Thr Cys Lys Asn Ser Pro Leu Asp Glu Leu Glu Glu
 1      5      10      15
Gly Glu Ile Arg Ser Asp Ser Glu Thr Ser Lys Pro Gln Glu Ser Phe
      20      25      30
Glu Lys Asn Ser Lys Arg Arg Val Ser Ala Asp Val Arg Lys Ser Lys
      35      40      45
Thr Ile Pro Arg Arg Gly Lys Ser Thr Val Cys Leu Asp Lys Asp Ser
      50      55      60
Arg Lys Thr His Val Arg Ile His Gln Thr Asn Asn Lys Trp Asn Lys
      65      70      75      80
Arg Pro Asp Lys Ser Ser Arg Ser Ser Lys Thr Glu Lys Lys Asp Lys
      85      90      95
Val Met Ser Thr Ser Ser Leu Glu Lys Ile Val Pro Ile Ile Ala Val
      100      105      110
Pro Ser Ser Glu Gln Glu Ile Met His Met Leu Arg Met Ile Arg Lys
      115      120      125

```

His Val Arg Lys Asn Tyr Met Lys Phe Lys Ala Lys Phe Ser Leu Ile  
 130 135 140  
 Gln Phe His Arg Ile Ile Glu Ser Ala Ile Leu Ser Phe Thr Ser Leu  
 145 150 155 160  
 Ile Lys His Leu Asn Leu His Lys Ile Ser Lys Ser Val Thr Thr Leu  
 165 170 175  
 Gln Lys Asn Leu Cys Asp Ile Ile Glu Ser Lys Leu Lys Gln Val Lys  
 180 185 190  
 Lys Asn Gly Ile Val Asp Arg Leu Phe Glu Gln Gln Leu Pro Asp Met  
 195 200 205  
 Lys Lys Lys Leu Trp Lys Phe Val Asp Asp Gln Leu Asp Tyr Leu Phe  
 210 215 220  
 Ala Lys Leu Arg Lys Ile Leu Val Cys Asp Ser Lys Ser Phe Gly Arg  
 225 230 235 240  
 Asp Ser Asp Glu Gly Lys Leu Glu Lys Thr Ser Lys Gln Asn Ala Gln  
 245 250 255  
 Tyr Ser Asn Arg Ser Glu Lys Gly Val Trp Asp Asn Ser Asn Arg Gly  
 260 265 270  
 Ile Ala Gly Lys Glu Lys Leu Ser Lys Ile Arg Lys Asp Pro Val His  
 275 280 285  
 Tyr Lys Ser Leu Xaa Val Gly Gly Val Lys Lys Ser Glu Glu Asn Tyr  
 290 295 300  
 Gln Asp Gln Asn Asn Ser Ser Ile Asn Thr Val Lys His Asp Ile Lys  
 305 310 315 320  
 Lys Asn Phe Asn Ile Cys Phe Asp Asn Ile Lys Asn Ser Gln Ser Glu  
 325 330 335  
 Glu Arg Ser Leu Glu Val His Cys Pro Ser Thr Pro Lys Ser Glu Lys  
 340 345 350  
 Asn Glu Gly Ser Ser Ile Glu Asp Ala Gln Thr Ser Gln His Ala Thr  
 355 360 365  
 Leu Lys Pro Glu Arg Ser Phe Glu Ile Leu Thr Glu Gln Gln Ala Ser  
 370 375 380  
 Ser Leu Thr Phe Asn Leu Val Ser Asp Ala Gln Met Gly Glu Ile Phe  
 385 390 395 400  
 Lys Ser Leu Leu Gln Gly Ser Asp Leu Leu Asn Ser Ser Val Asn Cys  
 405 410 415  
 Thr Glu Lys Ser Glu Trp Glu Leu Lys Thr Pro Glu Lys Gln Leu Leu  
 420 425 430  
 Glu Thr Leu Lys Cys Glu Ser Ile Pro Ala Cys Thr Thr Glu Glu Leu  
 435 440 445  
 Val Ser Gly Val Ala Ser Pro Cys Pro Lys Met Ile Ser Asp Asp Asn  
 450 455 460  
 Trp Ser Leu Leu Ser Ser Glu Lys Gly Pro Ser Leu Ser Ser Gly Leu  
 465 470 475 480  
 Ser Leu Pro Val His Pro Asp Val Leu Asp Glu Ser Cys Met Phe Glu  
 485 490 495  
 Val Ser Thr Asn Leu Pro Leu Ser Lys Asp Asn Val Cys Ser Val Glu  
 500 505 510  
 Lys Ser Lys Pro Cys Val Ser Ser Ile Leu Leu Glu Asp Leu Ala Val  
 515 520 525  
 Ser Leu Thr Val Pro Ser Pro Leu Lys Ser Asp Gly His Leu Ser Phe  
 530 535 540  
 Leu Lys Pro Asp Met Ser Ser Ser Ser Thr Pro Glu Glu Val Ile Ser  
 545 550 555 560  
 Ala His Phe Ser Glu Asp Ala Leu Leu Glu Gly Arg Gly Ile Ala Phe  
 565 570 575  
 Leu Ala Arg Tyr Phe Ile Leu Ala Leu Glu Ser Asp Asn Ser Ser Ser  
 580 585 590  
 Lys Ser Ser Cys Ser Ser Ser Trp Thr Ser Arg Ser Val Ala Pro Gly  
 595 600 605  
 Phe Gln Tyr His Pro Asn Leu Pro Met His Ala Val Ile Met Glu Lys  
 610 615 620  
 Ser Asn Asp His Phe Ile Val Lys Ile Arg Arg Ala Thr Pro Ser Thr

```

625          630          635          640
Ser Ser Gly Leu Lys Gln Ser Met Met Pro Asp Glu Leu Leu Thr Ser
          645          650          655
Leu Pro Arg His Gly Lys Glu Ala Asp Glu Gly Pro Glu Lys Glu Tyr
          660          665          670
Ile Ser Cys Gln Asn Thr Val Phe Lys Ser Val Glu Glu Leu Glu Asn
          675          680          685
Ser Asn Lys Asn Val Asp Gly Ser Lys Ser Thr His Glu Glu Gln Ser
          690          695          700
Ser Met Ile Gln Thr Gln Val Pro Asp Ile Tyr Glu Phe Leu Lys Asp
705          710          715          720
Ala Ser Asp Lys Met Gly His Ser Asp Glu Val Ala Asp Glu Cys Phe
          725          730          735
Lys Leu His Gln Val Trp Glu Thr Lys Val Pro Glu Ser Ile Glu Glu
          740          745          750
Leu Pro Ser Met Glu Glu Ile Ser His Ser Val Gly Glu His Leu Pro
          755          760          765
Asn Thr Tyr Val Asp Leu Thr Lys Asp Pro Val Thr Glu Thr Lys Asn
          770          775          780
Leu Gly Glu Phe Ile Glu Val Thr Val Leu His Ile Asp Gln Leu Gly
785          790          795          800
Cys Ser Gly Gly Asn Leu Asn Gln Ser Ala Gln Ile Leu Asp Asn Ser
          805          810          815
Leu Gln Ala Asp Thr Val Gly Ala Phe Ile Asp Leu Thr Gln Asp Ala
          820          825          830
Ser Ser Glu Ala Lys Ser Glu Gly Asn His Pro Ala Leu Ala Val Glu
          835          840          845
Asp Leu Gly Cys Gly Val Ile Gln Val Asp Glu Asp Asn Cys Lys Glu
          850          855          860
Glu Lys Ala Gln Val Ala Asn Arg Pro Leu Lys Cys Ile Val Glu Glu
865          870          875          880
Thr Tyr Ile Asp Leu Thr Thr Glu Ser Pro Ser Ser Cys Glu Val Lys
          885          890          895
Lys Asp Glu Leu Lys Ser Glu Pro Gly Ser Asn Cys Asp Asn Ser Glu
          900          905          910
Leu Pro Gly Thr Leu His Asn Ser His Lys Lys Arg Arg Asn Ile Ser
          915          920          925
Asp Leu Asn His Pro His Lys Lys Gln Arg Lys Glu Thr Asp Leu Thr
          930          935          940
Asn Lys Glu Lys Thr Lys Lys Pro Thr Gln Asp Ser Cys Glu Asn Thr
945          950          955          960
Glu Ala His Gln Lys Lys Ala Ser Lys Lys Lys Ala Pro Pro Val Thr
          965          970          975
Lys Asp Pro Ser Ser Leu Lys Ala Thr Pro Gly Ile Lys Asp Ser Ser
          980          985          990
Ala Ala Leu Ala Thr Ser Thr Ser Leu Ser Ala Lys Asn Val Ile Lys
          995          1000          1005
Lys Lys Gly Glu Ile Ile Ile Leu Trp Thr Arg Asn Asp Asp Arg Glu
1010          1015          1020
Ile Leu Leu Glu Cys Gln Lys Arg Gly Pro Ser Phe Lys Thr Phe Ala
1025          1030          1035          1040
Tyr Leu Ala Ala Lys Leu Asp Lys Asn Pro Asn Gln Val Ser Glu Arg
          1045          1050          1055
Phe Gln Gln Leu Met Lys Leu Phe Glu Lys Ser Lys Cys Arg
          1060          1065          1070

```

&lt;210&gt; 371

&lt;211&gt; 452

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(451)

&lt;223&gt; Xaa = any amino acid or nothing

&lt;400&gt; 371

```

Pro Ala Leu Leu Glu Phe Arg Thr Arg Leu Met Asp Leu Gly Gln Leu
 1          5          10          15
Arg Gly Val Pro Ala Tyr Arg Val His Val Xaa Arg Val Gly Ser Leu
          20          25          30
Leu Thr Gly Asp Ala Phe Thr His Val Xaa Leu Gly Gly Lys Asp Arg
          35          40          45
Lys Ile Tyr Cys Thr Asp Leu Arg Asn Pro Asp Ile Arg Val Leu Ile
          50          55          60
Cys Glu Glu Lys Ala Pro Val Leu Lys Met Glu Leu Asp Arg Ser Ala
          65          70          75          80
Asp Pro Pro Pro Ala Ile Trp Val Ala Thr Thr Lys Ser Thr Val Asn
          85          90          95
Lys Trp Thr Leu Lys Gly Ile His Asn Phe Arg Ala Ser Gly Asp Tyr
          100          105          110
Asp Asn Asp Cys Thr Asn Pro Ile Thr Pro Leu Cys Thr Gln Pro Asp
          115          120          125
Gln Val Ile Lys Gly Gly Ala Ser Ile Ile Gln Cys His Ile Leu Asn
          130          135          140
Asp Lys Arg His Ile Leu Thr Lys Asp Thr Asn Asn Asn Val Ala Tyr
          145          150          155          160
Trp Asp Val Leu Lys Ala Cys Lys Val Glu Asp Leu Gly Lys Val Asp
          165          170          175
Phe Glu Asp Glu Ile Lys Lys Arg Phe Lys Met Val Tyr Val Pro Asn
          180          185          190
Trp Phe Ser Val Asp Leu Lys Thr Gly Met Leu Thr Ile Thr Leu Asp
          195          200          205
Glu Ser Asp Cys Phe Ala Ala Trp Val Ser Ala Lys Asp Ala Gly Phe
          210          215          220
Ser Ser Pro Asp Gly Ser Asp Pro Lys Leu Asn Leu Gly Gly Leu Leu
          225          230          235          240
Leu Gln Ala Leu Leu Glu Tyr Trp Pro Arg Thr His Val Asn Pro Met
          245          250          255
Asp Glu Glu Glu Asn Glu Val Asn His Val Asn Gly Glu Gln Glu Asn
          260          265          270
Arg Val Gln Lys Gly Asn Gly Tyr Phe Gln Val Pro Pro His Thr Pro
          275          280          285
Val Ile Phe Gly Glu Ala Gly Gly Arg Thr Leu Phe Arg Leu Leu Cys
          290          295          300
Arg Asp Ser Gly Gly Glu Thr Glu Ser Met Leu Leu Asn Glu Thr Val
          305          310          315          320
Pro Gln Trp Val Ile Asp Ile Thr Val Asp Lys Asn Met Pro Lys Phe
          325          330          335
Asn Lys Ile Pro Phe Tyr Leu Gln Pro His Ala Ser Ser Gly Ala Lys
          340          345          350
Thr Leu Lys Lys Asp Arg Leu Ser Ala Ser Asp Met Leu Gln Val Arg
          355          360          365
Lys Val Met Glu His Val Tyr Glu Lys Ile Ile Asn Leu Asp Asn Glu
          370          375          380
Ser Gln Thr Thr Ser Ser Ser Asn Asn Glu Lys Pro Gly Glu Gln Glu
          385          390          395          400
Lys Glu Glu Asp Ile Ala Val Leu Ala Glu Glu Lys Ile Glu Leu Leu
          405          410          415
Cys Gln Asp Gln Val Leu Asp Pro Asn Met Asp Leu Arg Thr Val Lys
          420          425          430
His Phe Ile Trp Lys Ser Gly Gly Asp Leu Thr Leu His Tyr Arg Gln
          435          440          445
Lys Ser Thr
          450 451

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<210> 372  
 <211> 205  
 <212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(202)  
 <223> Xaa = any amino acid or nothing

<400> 372  
 Phe Lys Lys Ser Asn Lys Phe Xaa Tyr Lys Lys Cys Ser Asn Xaa Lys  
 1 5 10 15  
 Ser Ser Met Cys Arg Ser Ser Ser Arg Leu Asp Gly Ala Glu Xaa Ile  
 20 25 30  
 Ile Asn Glu Leu Lys Arg Gln Lys Thr Met His Thr Glu Ala Gln Arg  
 35 40 45  
 Asp Lys Gln Met Glu Asn Thr Glu Lys Ser Ile Arg Asp Leu Trp Asp  
 50 55 60  
 Arg Val Ser Arg Pro Asn Met Leu Leu Leu Glu Val Ser Glu Glu Glu  
 65 70 75 80  
 Asn Lys Glu Asn Gly Ile Glu Ala Ile Phe Glu Glu Ile Met Ala Val  
 85 90 95  
 Asn Phe Pro Lys Leu Xaa Lys Thr Ser Ser His Arg Leu Lys His Tyr  
 100 105 110  
 Glu Pro Gln Thr Gly Glu Ile Gln Arg Lys Tyr Lys Gln Leu Arg Xaa  
 115 120 125  
 Lys Arg Arg Ile Ile Phe Ser Gly Ala Thr Ala Trp Leu Thr Ala Asp  
 130 135 140  
 Phe Xaa Thr Lys Ala Met Glu Ser Arg Xaa Gln Trp Asn Glu Gln Cys  
 145 150 155 160  
 Arg Lys Glu Tyr Pro Ser Lys Ser Glu Gly Glu Leu Lys Met Phe Ser  
 165 170 175  
 Asp Lys Lys Asn Met Arg Lys Tyr Ile Ala Ser Arg Leu Ala Leu Lys  
 180 185 190  
 Glu Ile Leu Asn Gly Ile Ile Xaa Ala Glu  
 195 200 202

<210> 373  
 <211> 1081  
 <212> PRT  
 <213> Homo sapiens

<400> 373  
 Glu Asn Ala Val Gly Ser Trp Thr Asp Asp Leu Thr Gln Leu Ser Leu  
 1 5 10 15  
 Leu Lys Asp Thr Leu Ser Ala Tyr Ile Ser Ala Asp Asp Ile Ser Ile  
 20 25 30  
 Leu Asn Glu Arg Val Glu Leu Leu Gln Arg Gln Trp Glu Glu Leu Cys  
 35 40 45  
 His Gln Leu Ser Leu Arg Arg Gln Gln Ile Gly Glu Arg Leu Asn Glu  
 50 55 60  
 Trp Ala Val Phe Ser Glu Lys Asn Lys Glu Leu Cys Glu Trp Leu Thr  
 65 70 75 80  
 Gln Met Glu Ser Lys Val Ser Gln Asn Gly Asp Ile Leu Ile Glu Glu  
 85 90 95  
 Met Ile Glu Lys Leu Lys Lys Asp Tyr Gln Glu Glu Ile Ala Ile Ala  
 100 105 110  
 Gln Glu Asn Lys Ile Gln Leu Gln Gln Met Gly Glu Arg Leu Ala Lys

261

Leu Asp Asp Ser Arg Phe Gln Ile Gln Gln Thr Glu Asn Ile Ile Arg  
 625 630 635 640  
 Ser Lys Thr Pro Thr Gly Pro Glu Leu Asp Thr Ser Tyr Lys Gly Tyr  
 645 650 655  
 Met Lys Leu Leu Gly Glu Cys Ser Ser Ile Asp Ser Val Lys Arg  
 660 665 670  
 Leu Glu His Lys Leu Lys Glu Glu Glu Glu Ser Leu Pro Gly Phe Val  
 675 680 685  
 Asn Leu His Ser Thr Glu Thr Gln Thr Ala Gly Val Ile Asp Arg Trp  
 690 695 700  
 Glu Leu Leu Gln Ala Gln Ala Leu Ser Lys Glu Leu Arg Met Lys Gln  
 705 710 715 720  
 Asn Leu Gln Lys Trp Gln Gln Phe Asn Ser Asp Leu Asn Ser Ile Trp  
 725 730 735  
 Ala Trp Leu Gly Asp Thr Glu Glu Glu Leu Glu Gln Leu Gln Arg Leu  
 740 745 750  
 Glu Leu Ser Thr Asp Ile Gln Thr Ile Glu Leu Gln Ile Lys Lys Leu  
 755 760 765  
 Lys Glu Leu Gln Lys Ala Val Asp His Arg Lys Ala Ile Ile Leu Ser  
 770 775 780  
 Ile Asn Leu Cys Ser Pro Glu Phe Thr Gln Ala Asp Ser Lys Glu Ser  
 785 790 795 800  
 Arg Asp Leu Gln Asp Arg Leu Ser Gln Met Asn Gly Arg Trp Asp Arg  
 805 810 815  
 Val Cys Ser Leu Leu Glu Glu Trp Arg Gly Leu Leu Gln Asp Ala Leu  
 820 825 830  
 Met Gln Cys Gln Gly Phe His Glu Met Ser His Gly Leu Leu Leu Met  
 835 840 845  
 Leu Glu Asn Ile Asp Arg Arg Lys Asn Glu Ile Val Pro Ile Asp Ser  
 850 855 860  
 Asn Leu Asp Ala Glu Ile Leu Gln Asp His His Lys Gln Leu Met Gln  
 865 870 875 880  
 Ile Lys His Glu Leu Leu Glu Ser Gln Leu Arg Val Ala Ser Leu Gln  
 885 890 895  
 Asp Met Ser Cys Gln Leu Leu Val Asn Ala Glu Gly Thr Asp Cys Leu  
 900 905 910  
 Glu Ala Lys Glu Lys Val His Val Ile Gly Asn Arg Leu Lys Leu Leu  
 915 920 925  
 Leu Lys Glu Val Ser Arg His Ile Lys Glu Leu Glu Lys Leu Leu Asp  
 930 935 940  
 Val Ser Ser Ser Gln Gln Asp Leu Ser Ser Trp Ser Ser Ala Asp Glu  
 945 950 955 960  
 Leu Asp Thr Ser Gly Ser Val Ser Pro Thr Ser Gly Arg Ser Thr Pro  
 965 970 975  
 Asn Arg Gln Lys Thr Pro Arg Gly Lys Cys Ser Leu Ser Gln Pro Gly  
 980 985 990  
 Pro Ser Val Ser Ser Pro His Ser Arg Ser Thr Lys Gly Gly Ser Asp  
 995 1000 1005  
 Ser Ser Leu Ser Glu Pro Gly Pro Gly Arg Ser Gly Arg Gly Phe Met  
 1010 1015 1020  
 Phe Arg Val Leu Arg Ala Ala Leu Pro Leu Gln Leu Leu Leu Leu  
 1025 1030 1035 1040  
 Leu Ile Gly Leu Ala Cys Leu Val Pro Met Ser Glu Glu Asp Tyr Ser  
 1045 1050 1055  
 Cys Ala Leu Ser Asn Asn Phe Ala Arg Ser Phe His Pro Met Leu Arg  
 1060 1065 1070  
 Tyr Thr Asn Gly Pro Pro Pro Leu  
 1075 1080

&lt;210&gt; 374

&lt;211&gt; 814

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 374

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Met Asn Ala Val Gly Ser Pro Glu Gly Gln Glu Leu His Lys Leu Gly
 1          5          10          15
Ser Gly Ala Trp Asp Asn Pro Ala Tyr Ser Gly Pro Pro Ser Pro His
          20          25          30
Gly Thr Leu Arg Val Cys Thr Ile Ser Ser Thr Gly Pro Leu Gln Pro
          35          40          45
Gln Pro Lys Lys Pro Glu Asp Glu Pro Gln Glu Thr Ala Tyr Arg Thr
          50          55          60
Gln Val Ser Ser Cys Cys Leu His Ile Cys Gln Gly Ile Arg Gly Leu
65          70          75          80
Trp Gly Thr Thr Leu Thr Glu Asn Thr Ala Glu Asn Arg Glu Leu Tyr
          85          90          95
Ile Lys Thr Thr Leu Arg Glu Leu Leu Val Tyr Ile Val Phe Leu Val
          100          105          110
Asp Ile Cys Leu Leu Thr Tyr Gly Met Thr Ser Ser Ser Ala Tyr Tyr
          115          120          125
Tyr Thr Lys Val Met Ser Glu Leu Phe Leu His Thr Pro Ser Asp Thr
          130          135          140
Gly Val Ser Phe Gln Ala Ile Ser Ser Met Ala Asp Phe Trp Asp Phe
145          150          155          160
Ala Gln Gly Pro Leu Leu Asp Ser Leu Tyr Trp Thr Lys Trp Tyr Asn
          165          170          175
Asn Gln Ser Leu Gly His Gly Ser His Ser Phe Ile Tyr Tyr Glu Asn
          180          185          190
Met Leu Leu Gly Val Pro Arg Leu Arg Gln Leu Lys Val Arg Asn Asp
          195          200          205
Ser Cys Val Val His Glu Asp Phe Arg Glu Asp Ile Leu Ser Cys Tyr
210          215          220
Asp Val Tyr Ser Pro Asp Lys Glu Glu Gln Leu Pro Phe Gly Pro Phe
225          230          235          240
Asn Gly Thr Ala Trp Thr Tyr His Ser Gln Asp Glu Leu Gly Gly Phe
          245          250          255
Ser His Trp Gly Arg Leu Thr Ser Tyr Ser Gly Gly Gly Tyr Tyr Leu
          260          265          270
Asp Leu Pro Gly Ser Arg Gln Gly Ser Ala Glu Ala Leu Arg Ala Leu
          275          280          285
Gln Glu Gly Leu Trp Leu Asp Arg Gly Thr Arg Val Val Phe Ile Asp
          290          295          300
Phe Ser Val Tyr Asn Ala Asn Ile Asn Leu Phe Cys Val Leu Arg Leu
305          310          315          320
Val Val Glu Phe Pro Ala Thr Gly Gly Ala Ile Pro Ser Trp Gln Ile
          325          330          335
Arg Thr Val Lys Leu Ile Arg Tyr Val Ser Asn Trp Asp Phe Phe Ile
          340          345          350
Val Gly Cys Glu Val Ile Phe Cys Val Phe Ile Phe Tyr Tyr Val Val
          355          360          365
Glu Glu Ile Leu Glu Leu His Ile His Arg Leu Arg Tyr Leu Ser Ser
          370          375          380
Ile Trp Asn Ile Leu Asp Leu Val Val Ile Leu Leu Ser Ile Val Ala
385          390          395          400
Val Gly Phe His Ile Phe Arg Thr Leu Glu Val Asn Arg Leu Met Gly
          405          410          415
Lys Leu Leu Gln Gln Pro Asn Thr Tyr Ala Asp Phe Glu Phe Leu Ala
          420          425          430
Phe Trp Gln Thr Gln Tyr Asn Asn Met Asn Ala Val Asn Leu Phe Phe
          435          440          445
Ala Trp Ile Lys Ile Phe Lys Tyr Ile Ser Phe Asn Lys Thr Met Thr
          450          455          460
Gln Leu Ser Ser Thr Leu Ala Arg Cys Ala Lys Asp Ile Leu Gly Phe

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465          470          475          480
Ala Val Met Phe Phe Ile Val Phe Phe Ala Tyr Ala Gln Leu Gly Tyr
          485          490          495
Leu Leu Phe Gly Thr Gln Val Glu Asn Phe Ser Thr Phe Ile Lys Cys
          500          505          510
Ile Phe Thr Gln Phe Arg Ile Ile Leu Gly Asp Phe Asp Tyr Asn Ala
          515          520          525
Ile Asp Asn Ala Asn Arg Ile Leu Gly Pro Cys Pro Thr Leu Ser Pro
          530          535          540
Tyr Val Phe Phe Val Phe Phe Val Leu Leu Asn Met Phe Leu Ala Ile
545          550          555          560
Ile Asn Asp Thr Gln Tyr Ser Glu Val Lys Glu Glu Leu Ala Gly Gln
          565          570          575
Lys Asp Glu Leu Gln Leu Ser Asp Leu Leu Lys Gln Gly Tyr Asn Lys
          580          585          590
Thr Leu Leu Arg Leu Arg Leu Arg Lys Glu Arg Val Ser Asp Val Gln
          595          600          605
Lys Val Leu Gln Gly Gly Glu Gln Glu Ile Gln Phe Glu Asp Phe Thr
610          615          620
Asn Thr Leu Arg Glu Leu Gly His Ala Glu His Glu Ile Thr Glu Leu
625          630          635          640
Thr Ala Thr Phe Thr Lys Phe Asp Arg Asp Gly Asn Arg Ile Leu Asp
          645          650          655
Glu Lys Glu Gln Glu Lys Met Arg Gln Asp Leu Glu Glu Glu Arg Val
          660          665          670
Ala Leu Asn Thr Glu Ile Glu Lys Leu Gly Arg Ser Ile Val Ser Ser
          675          680          685
Pro Gln Gly Lys Ser Gly Pro Glu Ala Ala Arg Ala Gly Gly Trp Val
690          695          700
Ser Gly Glu Glu Phe Tyr Met Leu Thr Arg Arg Val Leu Gln Leu Glu
705          710          715          720
Thr Val Leu Glu Gly Val Val Ser Gln Ile Asp Ala Val Gly Ser Lys
          725          730          735
Leu Lys Met Leu Glu Arg Lys Gly Trp Leu Ala Pro Ser Pro Gly Val
          740          745          750
Lys Glu Gln Ala Ile Trp Lys His Pro Gln Pro Ala Pro Ala Val Thr
          755          760          765
Pro Asp Pro Trp Gly Val Gln Gly Gly Gln Glu Ser Glu Val Pro Tyr
770          775          780
Lys Arg Glu Glu Glu Ala Leu Glu Glu Arg Arg Leu Ser Arg Gly Glu
785          790          795          800
Ile Pro Thr Leu Gln Arg Ser
          805          807

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<210> 375  
 <211> 280  
 <212> PRT  
 <213> Homo sapiens

```

<400> 375
Asp Asp Gly Ala Ala His Val Met His Arg Glu Val Trp Met Ala Val
 1          5          10          15
Phe Ser Tyr Leu Ser His Gln Asp Leu Cys Val Cys Met Arg Val Cys
          20          25          30
Arg Thr Trp Asn Arg Trp Cys Cys Asp Lys Arg Leu Trp Thr Arg Ile
          35          40          45
Asp Leu Asn His Cys Lys Ser Ile Thr Pro Leu Met Leu Ser Gly Ile
          50          55          60
Ile Arg Arg Gln Pro Val Ser Leu Asp Leu Ser Trp Thr Asn Ile Ser
          65          70          75          80
Lys Lys Gln Leu Ser Trp Leu Ile Asn Arg Leu Pro Gly Leu Arg Asp

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      85      90      95
Leu Val Leu Ser Gly Cys Ser Trp Ile Ala Val Ser Ala Leu Cys Ser
      100      105      110
Ser Ser Cys Pro Leu Leu Arg Thr Leu Asp Val Gln Trp Val Glu Gly
      115      120      125
Leu Lys Asp Ala Gln Met Arg Asp Leu Leu Ser Pro Pro Thr Asp Asn
      130      135      140
Arg Pro Gly Gln Met Asp Asn Arg Ser Lys Leu Arg Asn Ile Val Glu
      145      150      155      160
Leu Arg Leu Ala Gly Leu Asp Ile Thr Asp Ala Ser Leu Arg Leu Ile
      165      170      175
Ile Arg His Met Pro Leu Leu Ser Lys Leu His Leu Ser Tyr Cys Asn
      180      185      190
His Val Thr Asp Gln Ser Ile Asn Leu Leu Thr Ala Val Gly Thr Thr
      195      200      205
Thr Arg Asp Ser Leu Thr Glu Ile Asn Leu Ser Asp Cys Asn Lys Val
      210      215      220
Thr Asp Gln Cys Leu Ser Phe Phe Lys Arg Cys Gly Asn Ile Cys His
      225      230      235      240
Ile Asp Leu Arg Tyr Cys Lys Gln Val Thr Lys Glu Gly Cys Glu Gln
      245      250      255
Phe Ile Ala Glu Met Ser Val Ser Val Gln Phe Gly Gln Val Glu Glu
      260      265      270
Lys Leu Leu Gln Lys Leu Ser
      275      279

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<210> 376  
 <211> 225  
 <212> PRT  
 <213> Homo sapiens

```

    <400> 376
Ser Trp Pro Gly Gln Ala Glu Pro Ser Glu Arg Glu Phe Val Val Arg
  1      5      10      15
Glu Ala Ala Glu Thr Arg Gly Ser Glu Val Phe Glu Ile Met Asn Pro
      20      25      30
Val Tyr Ser Pro Gly Ser Ser Gly Val Pro Tyr Ala Asn Ala Lys Gly
      35      40      45
Ile Gly Tyr Pro Ala Gly Phe Pro Met Gly Tyr Ala Ala Ala Ala Pro
      50      55      60
Ala Tyr Ser Pro Asn Met Tyr Pro Gly Ala Asn Pro Thr Phe Gln Thr
      65      70      75      80
Gly Tyr Thr Pro Gly Thr Pro Tyr Lys Val Ser Cys Ser Pro Thr Ser
      85      90      95
Gly Ala Val Pro Pro Tyr Ser Ser Ser Pro Asn Pro Tyr Gln Thr Ala
      100      105      110
Val Tyr Pro Val Arg Ser Ala Tyr Pro Gln Gln Ser Pro Tyr Ala Gln
      115      120      125
Gln Gly Thr Tyr Tyr Thr Gln Pro Leu Tyr Ala Ala Pro Pro His Val
      130      135      140
Ile His His Thr Thr Val Val Gln Pro Asn Gly Met Pro Ala Thr Val
      145      150      155      160
Tyr Pro Ala Pro Ile Pro Pro Pro Arg Gly Asn Gly Val Thr Met Gly
      165      170      175
Met Val Ala Gly Thr Thr Met Ala Met Ser Ala Gly Thr Leu Leu Thr
      180      185      190
Ala His Ser Pro Thr Pro Val Ala Pro His Pro Val Thr Val Pro Thr
      195      200      205
Tyr Arg Ala Gln Gly Thr Pro Thr Tyr Ser Tyr Val Pro Pro Gln Trp
      210      215      220      224

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<210> 377  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<400> 377  
 Val Thr Ala Ile Ile Asp Gly Thr Gly Ser Ile Gly Thr Ala Leu Gly  
 1 5 10 15  
 Pro Leu Leu Ala Gly Leu Ile Ser Pro Thr Gly Trp Asn Asn Val Phe  
 20 25 30  
 Tyr Met Leu Ile Ser Ala Asp Val Leu Ala Cys Leu Leu Leu Cys Arg  
 35 40 45  
 Leu Val Tyr Lys Glu Ile Leu Ala Trp Lys Val Ser Leu Ser Arg Gly  
 50 55 60  
 Ser Gly Tyr Lys Glu Ile  
 65 70

<210> 378  
 <211> 346  
 <212> PRT  
 <213> Homo sapiens

<221> misc\_feature  
 <222> (1)...(346)  
 <223> Xaa = any amino acid or nothing

<400> 378  
 Asn Ser Ser Ala Leu Lys Gly Leu Val Met Val Lys Ala Ala Thr Asp  
 1 5 10 15  
 Ser Arg Lys Gly Met Ala Phe Cys Ser Val Thr Xaa Pro Cys Cys Ser  
 20 25 30  
 Thr Leu Gln Glu Val Leu Asn His Ser Asp His His Pro Ile Leu Phe  
 35 40 45  
 Leu Ser Asn Leu Val Glu Gly Thr Tyr Thr Phe His Leu Lys Val Thr  
 50 55 60  
 Asp Ala Lys Gly Glu Ser Asp Thr Asp Arg Thr Thr Val Glu Val Lys  
 65 70 75 80  
 Pro Asp Pro Arg Lys Asn Asn Leu Val Glu Ile Ile Leu Asp Ile Asn  
 85 90 95  
 Val Ser Gln Leu Thr Glu Arg Leu Lys Gly Met Phe Ile Arg Gln Ile  
 100 105 110  
 Gly Val Leu Leu Gly Val Leu Asp Ser Asp Ile Ile Val Gln Lys Ile  
 115 120 125  
 Gln Pro Tyr Thr Glu Gln Ser Thr Lys Met Val Phe Phe Val Gln Asn  
 130 135 140  
 Glu Pro Pro His Gln Ile Phe Lys Gly His Glu Val Ala Ala Met Leu  
 145 150 155 160  
 Lys Ser Glu Leu Arg Lys Gln Lys Ala Asp Phe Leu Ile Phe Arg Ala  
 165 170 175  
 Leu Glu Val Asn Thr Val Thr Cys Gln Leu Asn Cys Ser Asp His Gly  
 180 185 190  
 His Cys Asp Ser Phe Thr Lys Arg Cys Ile Cys Asp Pro Phe Trp Met  
 195 200 205  
 Glu Asn Phe Ile Lys Val Gln Leu Arg Asp Gly Asp Ser Asn Cys Glu  
 210 215 220  
 Trp Ser Val Leu Tyr Val Ile Ile Ala Thr Phe Val Ile Val Val Ala  
 225 230 235 240

```

Leu Gly Ile Leu Ser Trp Thr Val Ile Cys Cys Cys Lys Arg Gln Lys
      245      250      255
Gly Lys Pro Lys Arg Lys Ser Lys Tyr Lys Ile Leu Asp Ala Thr Asp
      260      265      270
Gln Glu Ser Leu Glu Leu Lys Pro Thr Ser Arg Ala Gly Ile Lys Gln
      275      280      285
Lys Gly Leu Leu Leu Ser Ser Ser Leu Met His Ser Glu Ser Glu Leu
      290      295      300
Asp Ser Asp Asp Ala Ile Phe Thr Trp Pro Asp Arg Glu Lys Gly Lys
      305      310      315      320
Leu Leu His Gly Gln Asn Gly Ser Val Pro Asn Gly Gln Thr Pro Leu
      325      330      335
Lys Ala Arg Ser Pro Arg Glu Glu Ile Leu
      340      345 346

```

&lt;210&gt; 379

&lt;211&gt; 282

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(282)

&lt;223&gt; Xaa = any amino acid or nothing

&lt;400&gt; 379

```

Ile Ile Glu Lys Leu Ala Glu Gly Leu Asp Ile Gln Leu Lys Ser Pro
  1      5      10      15
Val Gln Cys Ile Asp Tyr Pro Gly Asp Glu Val Gln Val Thr Thr
      20      25      30
Asp Gly Thr Gly Tyr Ser Ala Gln Lys Val Leu Val Thr Val Pro Leu
      35      40      45
Ala Leu Leu Gln Lys Gly Ala Ile Gln Phe Asn Pro Pro Leu Ser Glu
      50      55      60
Lys Lys Met Lys Ala Ile Asn Ser Leu Gly Ala Gly Ile Ile Glu Lys
      65      70      75      80
Ile Ala Leu Gln Phe Pro Tyr Arg Phe Trp Asp Ser Lys Val Gln Gly
      85      90      95
Ala Asp Phe Phe Gly His Val Pro Pro Ser Ala Ser Lys Arg Gly Leu
      100      105      110
Phe Ala Val Phe Tyr Asp Met Asp Pro Gln Lys Lys His Ser Val Leu
      115      120      125
Met Ser Val Ile Ala Gly Glu Ala Val Ala Ser Val Arg Thr Leu Asp
      130      135      140
Asp Lys Gln Val Leu Gln Gln Cys Met Ala Thr Leu Arg Gly Leu Phe
      145      150      155      160
Lys Glu Gln Glu Val Pro Asp Pro Thr Lys Tyr Phe Val Thr Arg Trp
      165      170      175
Ser Thr Asp Pro Trp Ile Gln Met Ala Tyr Ser Phe Val Lys Thr Gly
      180      185      190
Gly Ser Gly Glu Ala Tyr Asp Ile Ile Ala Glu Asp Ile Gln Gly Thr
      195      200      205
Val Phe Phe Ala Gly Glu Ala Thr Asn Arg His Phe Pro Gln Thr Val
      210      215      220
Thr Gly Ala Tyr Leu Ser Gly Val Arg Glu Ala Ser Lys Ile Ala Ala
      225      230      235      240
Phe Xaa Glu Phe Gly Gly Pro Ser Phe Leu Leu Tyr Pro Arg Trp Gly
      245      250      255
Asn Leu Asn His Met Leu Asn Leu Ser Phe Ile Arg Gly Gly Lys Asn
      260      265      270
Arg Leu Tyr Ile Val Lys Leu Lys Cys Phe
      275      280      282

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<210> 380  
 <211> 109  
 <212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(107)  
 <223> Xaa = any amino acid or nothing

<400> 380  
 Glu Tyr Arg Arg Leu Glu Gln Gly Xaa Pro Asn Asp Ile Tyr Ile Leu  
 1 5 10 15  
 Tyr Pro Lys Thr Val Glu Gly Thr Ser Phe Pro Ser Ala Pro Gly Thr  
 20 25 30  
 Leu Thr Lys Thr Asp His Ile Ala Gly Ser Arg Asn Met Gln Asn Met  
 35 40 45  
 Phe Ser Asp His Asn Xaa Ser Glu Lys Xaa Ile Thr Lys Ile Xaa His  
 50 55 60  
 Lys Glu Pro Pro Tyr Ile Gln Lys Leu Asn Thr Leu Leu Asn Asn Ser  
 65 70 75 80  
 Arg Val Lys Glu Glu Ile Thr Arg Glu Ile Arg Lys Tyr Leu Gly Leu  
 85 90 95  
 Asn Asp Lys Asn Tyr Xaa Asn Val Trp Asp Ala  
 100 105 107

<210> 381  
 <211> 469  
 <212> PRT  
 <213> Homo sapiens

<400> 381  
 Leu Gln Gln Thr Glu Asp Lys Ser Leu Leu Asn Gln Gly Ser Ser Ser  
 1 5 10 15  
 Glu Glu Val Ala Gly Ser Ser Gln Lys Met Gly Gln Pro Gly Pro Ser  
 20 25 30  
 Gly Asp Ser Asp Leu Ala Thr Ala Leu His Arg Leu Ser Leu Arg Arg  
 35 40 45  
 Gln Asn Tyr Leu Ser Glu Lys Gln Phe Phe Ala Glu Trp Gln Arg  
 50 55 60  
 Lys Ile Gln Val Leu Ala Asp Gln Lys Glu Gly Val Ser Gly Cys Val  
 65 70 75 80  
 Thr Pro Thr Glu Ser Leu Ala Ser Leu Cys Thr Thr Gln Ser Glu Ile  
 85 90 95  
 Thr Asp Leu Ser Ser Ala Ser Cys Leu Arg Gly Phe Met Pro Glu Lys  
 100 105 110  
 Leu Gln Ile Val Lys Pro Leu Glu Gly Ser Gln Thr Leu Tyr His Trp  
 115 120 125  
 Gln Gln Leu Ala Gln Pro Asn Leu Gly Thr Ile Leu Asp Pro Arg Pro  
 130 135 140  
 Gly Val Ile Thr Lys Gly Phe Thr Gln Leu Pro Gly Asp Ala Ile Tyr  
 145 150 155 160  
 His Ile Ser Asp Leu Glu Glu Asp Glu Glu Gly Ile Thr Phe Gln  
 165 170 175  
 Val Gln Gln Pro Leu Glu Val Glu Glu Lys Leu Ser Thr Ser Lys Pro  
 180 185 190  
 Val Thr Gly Ile Phe Leu Pro Pro Ile Thr Ser Ala Gly Gly Pro Val  
 195 200 205  
 Thr Val Ala Thr Ala Asn Pro Gly Lys Cys Leu Ser Cys Thr Asn Ser

```

      210              215              220
Thr Phe Thr Phe Thr Thr Cys Arg Ile Leu His Pro Ser Asp Ile Thr
225              230              235              240
Gln Val Thr Pro Ser Ser Gly Phe Pro Ser Leu Ser Cys Gly Ser Ser
      245              250              255
Gly Ser Ser Ser Asn Thr Ala Val Asn Ser Pro Ala Leu Ala Tyr
      260              265              270
Arg Leu Ser Ile Gly Glu Ser Ile Thr Asn Arg Arg Asp Ser Thr Thr
      275              280              285
Thr Phe Ser Ser Thr Met Ser Leu Ala Lys Leu Leu Gln Glu Arg Gly
      290              295              300
Ile Ser Ala Lys Val Tyr His Ser Pro Ile Ser Glu Asn Pro Leu Gln
305              310              315              320
Pro Leu Pro Lys Ser Leu Ala Ile Pro Ser Thr Pro Pro Asn Ser Pro
      325              330              335
Ser His Ser Pro Cys Pro Ser Pro Leu Pro Phe Glu Pro Arg Val His
      340              345              350
Leu Ser Glu Asn Phe Leu Ala Ser Arg Pro Ala Glu Thr Phe Leu Gln
      355              360              365
Glu Met Tyr Gly Leu Arg Pro Ser Arg Asn Pro Pro Asp Val Gly Gln
      370              375              380
Leu Lys Met Asn Leu Val Asp Arg Leu Lys Arg Leu Gly Ile Ala Arg
385              390              395              400
Val Val Lys Asn Pro Gly Ala Gln Glu Asn Gly Arg Cys Gln Glu Ala
      405              410              415
Glu Ile Gly Pro Gln Lys Pro Asp Ser Ala Val Tyr Leu Asn Ser Gly
      420              425              430
Ser Ser Leu Leu Gly Gly Leu Arg Arg Asn Gln Ser Leu Pro Val Ile
      435              440              445
Met Gly Ser Phe Ala Ala Pro Val Cys Thr Ser Ser Pro Lys Met Gly
      450              455              460
Val Leu Lys Glu Asp
465              469

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<210> 382
<211> 669
<212> PRT
<213> Homo sapiens

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      <400> 382
Ser Ser Gly Ala Pro Ala Ala Gly Ala Ala Pro Ala Met Gly Glu Glu
  1              5              10              15
Asp Tyr Tyr Leu Glu Leu Cys Glu Arg Pro Val Gln Phe Glu Lys Ala
      20              25              30
Asn Pro Val Asn Cys Val Phe Phe Asp Glu Ala Asn Lys Gln Val Phe
      35              40              45
Ala Val Arg Ser Gly Gly Ala Thr Gly Val Val Val Lys Gly Pro Asp
      50              55              60
Asp Arg Asn Pro Ile Ser Phe Arg Met Asp Asp Lys Gly Glu Val Lys
      65              70              75              80
Cys Ile Lys Phe Ser Leu Glu Asn Lys Ile Leu Ala Val Gln Arg Thr
      85              90              95
Ser Lys Thr Val Asp Phe Cys Asn Phe Ile Pro Asp Asn Ser Gln Leu
      100              105              110
Glu Tyr Thr Gln Glu Cys Lys Thr Lys Asn Ala Asn Ile Leu Gly Phe
      115              120              125
Cys Trp Thr Ser Ser Thr Glu Ile Val Phe Ile Thr Asp Gln Gly Ile
      130              135              140
Glu Phe Tyr Gln Val Leu Pro Glu Lys Arg Ser Leu Lys Leu Leu Lys
      145              150              155              160
Ser His Asn Leu Asn Val Asn Trp Tyr Met Tyr Cys Pro Glu Ser Ala

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165      170      175
Val Ile Leu Leu Ser Thr Thr Val Leu Glu Asn Val Leu Gln Pro Phe
180      185      190
His Phe Arg Ala Gly Thr Met Ser Lys Leu Pro Lys Phe Glu Ile Glu
195      200      205
Leu Pro Ala Ala Pro Lys Ser Thr Lys Pro Ser Leu Ser Glu Arg Asp
210      215      220
Ile Ala Met Ala Thr Ile Tyr Gly Gln Leu Tyr Val Leu Phe Leu Arg
225      230      235      240
His His Ser Arg Thr Ser Asn Ser Thr Gly Ala Glu Val Val Leu Tyr
245      250      255
His Leu Pro Arg Glu Gly Ala Cys Lys Lys Met His Ile Leu Lys Leu
260      265      270
Asn Arg Thr Gly Lys Phe Ala Leu Asn Val Val Asp Asn Leu Val Val
275      280      285
Val His His Gln Asp Thr Glu Thr Ser Val Ile Phe Asp Ile Lys Leu
290      295      300
Arg Gly Glu Phe Asp Gly Ser Val Thr Phe His His Pro Val Leu Pro
305      310      315      320
Ala Arg Ser Ile Gln Pro Tyr Gln Ile Pro Ile Thr Gly Pro Ala Ala
325      330      335
Val Thr Ser Gln Ser Pro Val Pro Cys Lys Leu Tyr Ser Ser Ser Trp
340      345      350
Ile Val Phe Gln Pro Asp Ile Ile Ile Ser Ala Ser Gln Gly Tyr Leu
355      360      365
Trp Asn Leu Gln Val Lys Leu Glu Pro Ile Val Asn Leu Leu Pro Asp
370      375      380
Lys Gly Arg Leu Met Asp Phe Leu Leu Gln Arg Lys Glu Cys Lys Met
385      390      395      400
Val Ile Leu Ser Val Cys Ser Gln Met Leu Ser Glu Ser Asp Arg Ala
405      410      415
Ser Leu Pro Val Ile Ala Thr Val Phe Asp Lys Leu Asn His Glu Tyr
420      425      430
Lys Lys Tyr Leu Asp Ala Glu Gln Ser Tyr Ala Met Ala Val Glu Ala
435      440      445
Gly Gln Ser Arg Ser Ser Pro Leu Leu Lys Arg Pro Val Arg Thr Gln
450      455      460
Ala Val Leu Asp Gln Ser Asp Val Tyr Thr His Val Leu Ser Ala Phe
465      470      475      480
Val Glu Lys Lys Glu Met Pro His Lys Phe Val Ile Ala Val Leu Met
485      490      495
Glu Tyr Ile Arg Ser Leu Asn Gln Phe Gln Ile Ala Val Gln His Tyr
500      505      510
Leu His Glu Leu Val Ile Lys Thr Leu Val Gln His Asn Leu Phe Tyr
515      520      525
Met Leu His Gln Phe Leu Gln Tyr His Val Leu Ser Asp Ser Lys Pro
530      535      540
Leu Ala Cys Leu Leu Leu Ser Leu Glu Ser Phe Tyr Pro Pro Ala His
545      550      555      560
Gln Leu Ser Leu Asp Met Leu Lys Arg Leu Ser Thr Ala Asn Asp Glu
565      570      575
Ile Val Glu Val Leu Leu Ser Lys His Gln Val Leu Ala Ala Leu Arg
580      585      590
Phe Ile Arg Gly Ile Gly Gly His Asp Asn Ile Ser Ala Arg Lys Phe
595      600      605
Leu Asp Ala Ala Lys Gln Thr Glu Asp Asn Met Leu Phe Tyr Thr Ile
610      615      620
Phe Arg Phe Phe Glu Gln Arg Asn Gln Arg Leu Arg Gly Ser Pro Asn
625      630      635      640
Phe Thr Pro Gly Glu His Cys Glu Glu His Val Ala Phe Phe Lys Gln
645      650      655
Ile Phe Gly Asp Gln Ala Leu Met Arg Pro Thr Thr Phe
660      665      669

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<210> 383  
 <211> 343  
 <212> PRT  
 <213> Homo sapiens

<400> 383  
 Thr Leu Asn Tyr Pro Ala Glu Asn Ser Phe Asn His Arg Pro Tyr Thr  
 1 5 10 15  
 Ala Cys Asp Phe Ile Glu Gly Ile Tyr Arg Thr Glu Arg Asp Lys Gly  
 20 25 30  
 Thr Leu Tyr Glu Leu Thr Phe Lys Gly Asp His Lys His Glu Phe Lys  
 35 40 45  
 Arg Leu Ile Leu Phe Arg Pro Phe Gly Pro Ile Met Lys Val Lys Asn  
 50 55 60  
 Glu Lys Leu Asn Met Ala Asn Thr Leu Ile Asn Val Ile Val Pro Leu  
 65 70 75 80  
 Ala Lys Arg Val Asp Lys Phe Arg Gln Phe Met Gln Asn Phe Arg Glu  
 85 90 95  
 Met Cys Ile Glu Gln Asp Gly Arg Val His Leu Thr Val Val Tyr Phe  
 100 105 110  
 Gly Lys Glu Glu Ile Asn Glu Val Lys Gly Ile Leu Glu Asn Thr Ser  
 115 120 125  
 Lys Ala Ala Asn Phe Arg Asn Phe Thr Phe Ile Gln Leu Asn Gly Glu  
 130 135 140  
 Phe Ser Arg Gly Lys Gly Leu Asp Val Gly Ala Arg Phe Trp Lys Gly  
 145 150 155 160  
 Ser Asn Val Leu Leu Phe Phe Cys Asp Val Asp Ile Tyr Phe Thr Ser  
 165 170 175  
 Glu Phe Leu Asn Thr Cys Arg Leu Asn Thr Gln Pro Gly Lys Lys Val  
 180 185 190  
 Phe Tyr Pro Val Leu Phe Ser Gln Tyr Asn Pro Gly Ile Ile Tyr Gly  
 195 200 205  
 His His Asp Ala Val Pro Pro Leu Glu Gln Gln Leu Val Ile Lys Lys  
 210 215 220  
 Glu Thr Gly Phe Trp Arg Asp Phe Gly Phe Gly Met Thr Cys Gln Tyr  
 225 230 235 240  
 Arg Ser Asp Phe Ile Asn Ile Gly Gly Phe Asp Leu Asp Ile Lys Gly  
 245 250 255  
 Trp Gly Gly Glu Asp Val His Leu Tyr Arg Lys Tyr Leu His Ser Asn  
 260 265 270  
 Leu Ile Val Val Arg Thr Pro Val Arg Gly Leu Phe His Leu Trp His  
 275 280 285  
 Glu Lys Arg Cys Met Asp Glu Leu Thr Pro Glu Gln Tyr Lys Met Cys  
 290 295 300  
 Met Gln Ser Lys Ala Met Asn Glu Ala Ser His Gly Gln Leu Gly Met  
 305 310 315 320  
 Leu Val Phe Arg His Glu Ile Glu Ala His Leu Arg Lys Gln Lys Gln  
 325 330 335  
 Lys Thr Ser Ser Lys Lys Thr  
 340 343

<210> 384  
 <211> 99  
 <212> PRT  
 <213> Homo sapiens

<400> 384  
 Phe Leu Lys Val Glu Ile Ser Ile Gln Ser Asn Phe Gln Pro Gly Met

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      1           5           10           15
Lys Leu Glu Val Ala Asn Lys Asn Asn Pro Asp Thr Tyr Trp Val Ala
      20           25           30
Thr Ile Ile Thr Thr Cys Gly Gln Leu Leu Leu Leu Arg Tyr Cys Gly
      35           40           45
Tyr Gly Glu Asp Arg Arg Ala Asp Phe Trp Cys Asp Val Val Ile Ala
      50           55           60
Asp Leu His Pro Val Gly Trp Cys Thr Gln Asn Asn Lys Val Leu Met
      65           70           75           80
Pro Pro Asp Gly Glu Pro Leu Phe Gln Arg Leu Arg Phe Thr Ser Arg
      85           90           95
His Pro Ser
      99

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<210> 385  
 <211> 93  
 <212> PRT  
 <213> Homo sapiens

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      <400> 385
Ser Leu Gly Trp Gly Leu Asp Ile Leu Gln Leu Leu Asp Leu Phe Ile
      1           5           10           15
Gln Trp Asp Trp Ser Thr Tyr Leu Ala Asp Tyr Gly Gln Pro Asn Cys
      20           25           30
Lys Tyr Leu Arg Val Asn Pro Val Thr Ala Leu Thr Leu Leu Glu Lys
      35           40           45
Ile Ser Arg Glu Met Lys Asp Thr Ser Arg Lys Asn Asn Met Phe Ala
      50           55           60
Gln Phe Arg Lys Asn Glu Arg Asp Lys Gln Lys Leu Ile Asp Ser Val
      65           70           75           80
Ala Lys Gln Leu Arg Gly Leu Ile Ser Ser His His Ser
      85           90           93

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<210> 386  
 <211> 150  
 <212> PRT  
 <213> Homo sapiens

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      <400> 386
Gly Gln Asp Asp Thr Ser Lys Ala Asp Lys Pro Lys Val Asp Glu Glu
      1           5           10           15
Gly Asp Glu Asn Glu Asp Asp Lys Asp Tyr His Arg Ser Asp Pro Gln
      20           25           30
Ile Ala Ile Cys Leu Asp Cys Leu Arg Asn Asn Gly Gln Ser Gly Asp
      35           40           45
Asn Val Val Lys Gly Leu Met Lys Lys Phe Ile Arg Cys Ser Thr Arg
      50           55           60
Val Thr Val Gly Thr Ile Lys Lys Phe Leu Ser Leu Lys Leu Lys Leu
      65           70           75           80
Pro Ser Ser Tyr Glu Leu Asp Val Leu Cys Asn Gly Glu Ile Met Gly
      85           90           95
Lys Asp His Thr Met Glu Phe Ile Tyr Met Thr Arg Trp Arg Leu Arg
      100          105          110
Gly Glu Asn Phe Arg Cys Leu Asn Cys Ser Ala Ser Gln Val Cys Ser
      115          120          125
Gln Asp Gly Pro Leu Tyr Gln Ser Tyr Pro Met Val Leu Gln Tyr Arg
      130          135          140
Pro Arg Ile Asp Phe Gly
      145          150

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<210> 387  
 <211> 724  
 <212> PRT  
 <213> Homo sapiens

<400> 387  
 Gly Glu Lys Gly Gly Met Lys Pro Pro Ala His Trp Thr Gly Gly Leu  
 1 . 5 10 15  
 Gln Pro Glu Leu Gln Gly Ser Pro Ala Gly Trp Asp Ser Thr Glu Gly  
 20 25 30  
 Trp Thr Trp Gly Asp Gly Glu His Gly Leu Gly Ala Ala Ala Met Pro  
 35 40 45  
 Thr Trp Gly Ala Arg Pro Ala Ser Pro Asp Arg Phe Ala Val Ser Ala  
 50 55 60  
 Glu Ala Glu Asn Lys Val Arg Glu Gln Gln Pro His Val Glu Arg Ile  
 65 70 75 80  
 Phe Ser Val Gly Val Ser Val Leu Pro Lys Asp Cys Pro Asp Asn Pro  
 85 90 95  
 His Ile Trp Leu Gln Leu Glu Gly Pro Lys Glu Asn Ala Ser Arg Ala  
 100 105 110  
 Lys Glu Tyr Leu Lys Gly Leu Cys Ser Pro Glu Leu Gln Asp Glu Ile  
 115 120 125  
 His Tyr Pro Pro Lys Leu His Cys Ile Phe Leu Gly Ala Gln Gly Phe  
 130 135 140  
 Phe Leu Asp Cys Leu Ala Trp Ser Thr Ser Ala His Leu Val Pro Arg  
 145 150 155 160  
 Ala Pro Gly Ser Leu Met Ile Ser Gly Leu Thr Glu Ala Phe Val Met  
 165 170 175  
 Ala Gln Ser Arg Val Glu Glu Leu Ala Glu Arg Leu Ser Trp Asp Phe  
 180 185 190  
 Thr Pro Gly Pro Ser Ser Gly Ala Ser Gln Cys Thr Gly Val Leu Arg  
 195 200 205  
 Asp Phe Ser Ala Leu Leu Gln Ser Pro Gly Asp Ala His Arg Glu Ala  
 210 215 220  
 Leu Leu Gln Leu Pro Leu Ala Val Gln Glu Glu Leu Leu Ser Leu Val  
 225 230 235 240  
 Gln Glu Ala Ser Ser Gly Gln Gly Pro Gly Ala Leu Ala Ser Trp Glu  
 245 250 255  
 Gly Arg Ser Ser Ala Leu Leu Gly Ala Gln Cys Gln Gly Val Arg Ala  
 260 265 270  
 Pro Pro Ser Asp Gly Arg Glu Ser Leu Asp Thr Gly Ser Met Gly Pro  
 275 280 285  
 Gly Asp Cys Arg Gly Ala Arg Gly Asp Thr Tyr Ala Val Glu Lys Glu  
 290 295 300  
 Gly Gly Thr Gln Gly Gly Pro Arg Glu Met Asp Leu Gly Trp Lys Glu  
 305 310 315 320  
 Leu Pro Gly Glu Glu Ala Trp Glu Arg Glu Val Ala Leu Arg Pro Gln  
 325 330 335  
 Ser Val Gly Gly Gly Ala Arg Glu Ser Ala Pro Leu Lys Gly Lys Ala  
 340 345 350  
 Leu Gly Lys Glu Glu Ile Ala Leu Gly Gly Gly Gly Phe Cys Val His  
 355 360 365  
 Arg Glu Pro Pro Gly Ala His Gly Ser Cys His Arg Ala Ala Gln Ser  
 370 375 380  
 Arg Gly Ala Ser Leu Leu Gln Arg Leu His Asn Gly Asn Ala Ser Pro  
 385 390 395 400  
 Pro Arg Val Pro Ser Pro Pro Pro Ala Pro Glu Pro Pro Trp His Cys  
 405 410 415  
 Gly Asp Arg Gly Asp Cys Gly Asp Arg Gly Asp Val Gly Asp Arg Gly  
 420 425 430

Asp Lys Gln Gln Gly Met Ala Arg Gly Arg Gly Pro Gln Trp Lys Arg  
                   435                  440                  445  
 Gly Ala Arg Gly Gly Asn Leu Val Thr Gly Thr Gln Arg Phe Lys Glu  
                   450                  455                  460  
 Ala Leu Gln Asp Pro Phe Thr Leu Cys Leu Ala Asn Val Pro Gly Gln  
 465                  470                  475                  480  
 Pro Asp Leu Arg His Ile Val Ile Asp Gly Ser Asn Val Ala Met Val  
                   485                  490                  495  
 His Gly Leu Gln His Tyr Phe Ser Ser Arg Gly Ile Ala Ile Ala Val  
                   500                  505                  510  
 Gln Tyr Phe Trp Asp Arg Gly His Arg Asp Ile Thr Val Phe Val Pro  
                   515                  520                  525  
 Gln Trp Arg Phe Ser Lys Asp Ala Lys Val Arg Glu Ser His Phe Leu  
                   530                  535                  540  
 Gln Lys Leu Tyr Ser Leu Ser Leu Leu Ser Leu Thr Pro Ser Arg Val  
 545                  550                  555                  560  
 Met Asp Gly Lys Arg Ile Ser Ser Tyr Asp Asp Arg Phe Met Val Lys  
                   565                  570                  575  
 Leu Ala Glu Glu Thr Asp Gly Ile Ile Val Ser Asn Asp Gln Phe Arg  
                   580                  585                  590  
 Asp Leu Ala Glu Glu Ser Glu Lys Trp Met Ala Ile Ile Arg Glu Arg  
                   595                  600                  605  
 Leu Leu Pro Phe Thr Phe Val Gly Asn Leu Phe Met Val Pro Asp Asp  
                   610                  615                  620  
 Pro Leu Gly Arg Asn Gly Pro Thr Leu Asp Glu Phe Leu Lys Lys Pro  
 625                  630                  635                  640  
 Ala Arg Thr Gln Gly Ser Ser Lys Ala Gln His Pro Ser Arg Gly Phe  
                   645                  650                  655  
 Ala Glu His Gly Lys Gln Gln Gln Gly Arg Glu Glu Glu Lys Gly Ser  
                   660                  665                  670  
 Gly Gly Ile Arg Lys Thr Arg Glu Thr Glu Arg Leu Arg Arg Gln Leu  
                   675                  680                  685  
 Leu Glu Val Phe Trp Gly Gln Asp His Lys Val Asp Phe Ile Leu Gln  
                   690                  695                  700  
 Arg Glu Pro Tyr Cys Arg Asp Ile Asn Gln Leu Ser Glu Ala Leu Leu  
 705                  710                  715                  720  
 Ser Leu Asn Phe  
                   724

<210> 388  
 <211> 446  
 <212> PRT  
 <213> Homo sapiens

<400> 388  
 Ile Asp Thr Gly Ser His Tyr Val Ala Gln Ala Gly Val Lys Leu Leu  
   1                  5                  10                  15  
 Gly Ser Ser Ser Tyr Pro Thr Ser Ala Ser Gln Ser Ala Leu Ile Thr  
                   20                  25                  30  
 Gly Leu Ser His Arg Ala Trp Pro Arg Tyr Ile Ser Leu Leu Thr Ser  
                   35                  40                  45  
 His Arg Tyr Glu Asn Gly Arg Gly Ser Ser His Gln Gln Gln Val Thr  
                   50                  55                  60  
 Cys Tyr Pro Phe Lys Asp Val Asn Asn Trp Trp Ile Val Lys Asp Pro  
                   65                  70                  75                  80  
 Arg Arg His Gln Leu Val Val Ser Ser Pro Pro Arg Pro Val Arg His  
                   85                  90                  95  
 Gly Asp Met Val Gln Leu Val His Gly Met Thr Thr Arg Ser Leu Asn  
                   100                  105                  110  
 Thr His Asp Val Ala Ala Pro Leu Ser Pro His Ser Gln Glu Val Ser  
                   115                  120                  125

Cys Tyr Ile Asp Tyr Asn Ile Ser Met Pro Ala Gln Asn Leu Trp Arg  
 130 135 140  
 Leu Glu Ile Val Asn Arg Gly Ser Asp Thr Asp Val Trp Lys Thr Ile  
 145 150 155 160  
 Leu Ser Glu Val Arg Phe Val His Val Asn Thr Ser Ala Val Leu Lys  
 165 170 175  
 Leu Ser Gly Ala His Leu Pro Asp Trp Gly Tyr Arg Gln Leu Glu Ile  
 180 185 190  
 Val Gly Glu Lys Leu Ser Arg Gly Tyr His Gly Ser Thr Val Trp Asn  
 195 200 205  
 Val Glu Glu His Arg Tyr Gly Ala Ser Gln Glu Gln Arg Glu Arg Glu  
 210 215 220  
 Arg Glu Leu His Ser Pro Ala Gln Val Asp Val Ser Arg Asn Leu Ser  
 225 230 235 240  
 Phe Met Ala Arg Phe Ser Glu Leu Gln Trp Arg Met Leu Ala Leu Arg  
 245 250 255  
 Ser Asp Asp Ser Glu His Lys Tyr Ser Ser Ser Pro Leu Glu Trp Val  
 260 265 270  
 Thr Leu Asp Thr Asn Ile Ala Tyr Trp Leu His Pro Arg Thr Ser Ala  
 275 280 285  
 Gln Ile His Leu Leu Gly Asn Ile Val Ile Trp Val Ser Gly Ser Leu  
 290 295 300  
 Ala Leu Ala Ile Tyr Ala Leu Leu Ser Leu Trp Tyr Leu Leu Arg Arg  
 305 310 315 320  
 Arg Arg Asn Val His Asp Leu Pro Gln Asp Ala Trp Leu Arg Trp Val  
 325 330 335  
 Leu Ala Gly Ala Leu Cys Ala Gly Gly Trp Ala Val Asn Tyr Leu Pro  
 340 345 350  
 Phe Phe Leu Met Glu Lys Thr Leu Phe Leu Tyr His Tyr Leu Pro Ala  
 355 360 365  
 Leu Thr Phe Gln Ile Leu Leu Pro Val Val Leu Gln His Ile Ser  
 370 375 380  
 Asp His Leu Cys Arg Ser Gln Leu Gln Arg Ser Ile Phe Ser Ala Leu  
 385 390 395 400  
 Val Val Ala Trp Tyr Ser Ser Ala Cys His Val Ser Asn Thr Leu Arg  
 405 410 415  
 Pro Leu Thr Tyr Gly Asp Lys Ser Leu Ser Pro His Glu Leu Lys Ala  
 420 425 430  
 Leu Arg Trp Lys Asp Ser Trp Asp Ile Leu Ile Arg Lys His  
 435 440 445 446

<210> 389  
 <211> 594  
 <212> PRT  
 <213> Homo sapiens

<400> 389  
 Glu Thr Asp Asn Asp Leu Thr Lys Glu Met Tyr Glu Gly Lys Glu Asn  
 1 5 10 15  
 Val Ser Phe Glu Leu Gln Arg Asp Phe Ser Gln Glu Thr Asp Phe Ser  
 20 25 30  
 Glu Ala Ser Leu Leu Glu Lys Gln Gln Glu Val His Ser Ala Gly Asn  
 35 40 45  
 Ile Lys Lys Glu Lys Ser Asn Thr Ile Asp Gly Thr Val Lys Asp Glu  
 50 55 60  
 Thr Ser Pro Val Glu Glu Cys Phe Phe Ser Gln Ser Ser Asn Ser Tyr  
 65 70 75 80  
 Gln Cys His Thr Ile Thr Gly Glu Gln Pro Ser Gly Cys Thr Gly Leu  
 85 90 95  
 Gly Lys Ser Ile Ser Phe Asp Thr Lys Leu Val Lys His Glu Ile Ile  
 100 105 110



Asn Ser Glu Glu Arg Pro Phe Lys Cys Glu Glu Leu Val Glu Pro Phe  
 115 120 125  
 Arg Cys Asp Ser Gln Leu Ile Gln His Gln Glu Asn Asn Thr Glu Glu  
 130 135 140  
 Lys Pro Tyr Gln Cys Ser Glu Cys Gly Lys Ala Phe Ser Ile Asn Glu  
 145 150 155 160  
 Lys Leu Ile Trp His Gln Arg Leu His Ser Gly Glu Lys Pro Phe Lys  
 165 170 175  
 Cys Val Glu Cys Gly Lys Ser Phe Ser Tyr Ser Ser His Tyr Ile Thr  
 180 185 190  
 His Gln Thr Ile His Ser Gly Glu Lys Pro Tyr Gln Cys Lys Met Cys  
 195 200 205  
 Gly Lys Ala Phe Ser Val Asn Gly Ser Leu Ser Arg His Gln Arg Ile  
 210 215 220  
 His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Glu Cys Gly Asn Gly Phe  
 225 230 235 240  
 Ser Cys Ser Ser Ala Tyr Ile Thr His Gln Arg Val His Thr Gly Glu  
 245 250 255  
 Lys Pro Tyr Glu Cys Asn Asp Cys Gly Lys Ala Phe Asn Gly Asn Ala  
 260 265 270  
 Lys Leu Ile Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Glu  
 275 280 285  
 Cys Asn Glu Cys Gly Lys Gly Phe Arg Cys Ser Ser Gln Leu Arg Gln  
 290 295 300  
 His Gln Ser Ile His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Glu Cys  
 305 310 315 320  
 Gly Lys Gly Phe Asn Asn Asn Thr Lys Leu Ile Gln His Gln Arg Ile  
 325 330 335  
 His Thr Gly Glu Lys Pro Tyr Glu Cys Thr Glu Cys Gly Lys Ala Phe  
 340 345 350  
 Ser Val Lys Gly Lys Leu Ile Gln His Gln Arg Ile His Thr Gly Glu  
 355 360 365  
 Lys Pro Tyr Glu Cys Asn Glu Cys Gly Lys Ala Phe Arg Cys Asn Ser  
 370 375 380  
 Gln Phe Arg Gln His Leu Arg Ile His Thr Gly Glu Lys Pro Tyr Glu  
 385 390 395 400  
 Cys Asn Glu Cys Gly Lys Ala Phe Ser Val Asn Gly Lys Leu Met Arg  
 405 410 415  
 His Gln Arg Ile His Thr Gly Glu Lys Pro Phe Glu Cys Asn Glu Cys  
 420 425 430  
 Gly Arg Cys Phe Thr Ser Lys Arg Asn Leu Leu Asp His His Arg Ile  
 435 440 445  
 His Thr Gly Glu Lys Pro Tyr Gln Cys Lys Glu Cys Gly Lys Ala Phe  
 450 455 460  
 Ser Ile Asn Ala Lys Leu Thr Arg His Gln Arg Ile His Thr Gly Glu  
 465 470 475 480  
 Lys Pro Phe Lys Cys Met Glu Cys Glu Lys Ala Phe Ser Cys Ser Ser  
 485 490 495  
 Asn Tyr Ile Val His Gln Arg Ile His Thr Gly Glu Lys Pro Phe Gln  
 500 505 510  
 Cys Lys Glu Cys Gly Lys Ala Phe His Val Asn Ala His Leu Ile Arg  
 515 520 525  
 His Gln Arg Ser His Thr Gly Glu Lys Pro Phe Arg Cys Val Glu Cys  
 530 535 540  
 Gly Lys Gly Phe Ser Phe Ser Ser Asp Tyr Ile Ile His Gln Thr Val  
 545 550 555 560  
 His Thr Trp Lys Lys Pro Tyr Met Cys Ser Val Cys Gly Lys Ala Phe  
 565 570 575  
 Arg Phe Ser Phe Gln Leu Ser Gln His Gln Ser Val His Ser Glu Gly  
 580 585 590  
 Lys Ser  
 594

<210> 390  
 <211> 472  
 <212> PRT  
 <213> Homo sapiens

<400> 390  
 Val Arg Thr Pro Tyr Asp Leu Asp Asn Ile Tyr Leu Glu Glu Val Asp  
 1 5 10 15  
 Ser Val Val Ala Glu Tyr Glu Leu Glu Tyr Leu Leu Leu Glu Gly  
 20 25 30  
 His Cys Tyr Asp Ile Thr Thr Gly Gln Pro Pro Arg Gly Leu Gln Phe  
 35 40 45  
 Thr Leu Gly Thr Ser Ala Asn Pro Val Ile Val Asp Thr Ile Val Met  
 50 55 60  
 Ala Asn Leu Gly Tyr Phe Gln Leu Lys Ala Asn Pro Gly Ala Trp Ile  
 65 70 75 80  
 Leu Arg Leu Arg Lys Gly Arg Ser Glu Asp Ile Tyr Arg Ile Tyr Ser  
 85 90 95  
 His Asp Gly Thr Asp Ser Pro Pro Asp Ala Asp Glu Val Val Ile Val  
 100 105 110  
 Leu Asn Asn Phe Lys Ser Lys Ile Ile Lys Val Lys Val Gln Lys Lys  
 115 120 125  
 Ala Asp Met Val Asn Glu Asp Leu Leu Ser Asp Gly Thr Ser Glu Asn  
 130 135 140  
 Glu Ser Gly Phe Trp Asp Ser Phe Lys Trp Gly Phe Thr Gly Gln Lys  
 145 150 155 160  
 Thr Glu Glu Val Lys Gln Asp Lys Asp Asp Ile Ile Asn Ile Phe Ser  
 165 170 175  
 Val Ala Ser Gly His Leu Tyr Glu Arg Phe Leu Arg Ile Met Met Leu  
 180 185 190  
 Ser Val Leu Lys Asn Thr Lys Thr Pro Val Lys Phe Trp Phe Leu Lys  
 195 200 205  
 Asn Tyr Leu Ser Pro Thr Phe Lys Glu Phe Ile Pro Tyr Met Ala Asn  
 210 215 220  
 Glu Tyr Asn Phe Gln Tyr Glu Leu Val Gln Tyr Lys Trp Pro Arg Trp  
 225 230 235 240  
 Leu His Gln Gln Thr Glu Lys Gln Arg Ile Ile Trp Gly Tyr Lys Ile  
 245 250 255  
 Leu Phe Leu Asp Val Leu Phe Pro Leu Val Val Asp Lys Phe Leu Phe  
 260 265 270  
 Val Asp Ala Asp Gln Ile Val Arg Thr Asp Leu Lys Glu Leu Arg Asp  
 275 280 285  
 Phe Asn Leu Asp Gly Ala Pro Tyr Gly Tyr Thr Pro Phe Cys Asp Ser  
 290 295 300  
 Arg Arg Glu Met Asp Gly Tyr Arg Phe Trp Lys Ser Gly Tyr Trp Ala  
 305 310 315 320  
 Ser His Leu Ala Gly Arg Lys Tyr His Ile Ser Ala Leu Tyr Val Val  
 325 330 335  
 Asp Leu Lys Lys Phe Arg Lys Ile Ala Ala Gly Asp Arg Leu Arg Gly  
 340 345 350  
 Gln Tyr Gln Gly Leu Ser Gln Asp Pro Asn Ser Leu Ser Asn Leu Asp  
 355 360 365  
 Gln Asp Leu Pro Asn Asn Met Ile His Gln Val Pro Ile Lys Ser Leu  
 370 375 380  
 Pro Gln Glu Trp Leu Trp Cys Glu Thr Trp Cys Asp Asp Ala Ser Lys  
 385 390 395 400  
 Lys Arg Ala Lys Thr Ile Asp Leu Cys Asn Asn Pro Met Thr Lys Glu  
 405 410 415  
 Pro Lys Leu Glu Ala Ala Val Arg Ile Val Pro Glu Trp Gln Asp Tyr  
 420 425 430  
 Asp Gln Glu Ile Lys Gln Leu Gln Ile Arg Phe Gln Lys Glu Lys Glu

435                      440                      445  
 Thr Gly Ala Leu Cys Gln Arg Glu Ala Gln Lys Asn Pro Ser Arg Lys  
 450                      455                      460  
 Gly Pro Gln Lys Arg Glu Glu Leu  
 465                      470                      472

<210> 391  
 <211> 203  
 <212> PRT  
 <213> Homo sapiens

<400> 391  
 Arg Cys Ala Val Leu Phe Cys Ser Ser Cys Ser Lys Val Ile Gln Val  
 1                      5                      10                      15  
 Gly Gln Val His Gly Gly Leu Met Gly Ile Ile Gln Arg Ala Met Val  
 20                      25                      30  
 Lys Ala Cys Pro His Val Trp Phe Glu Arg Ser Glu Met Lys Asp Arg  
 35                      40                      45  
 His Leu Val Thr Lys Arg Leu Lys Glu His Ile Ala Asp Lys Lys Lys  
 50                      55                      60  
 Leu Pro Ile Leu Ile Phe Pro Glu Gly Thr Cys Ile Asn Asn Thr Ser  
 65                      70                      75                      80  
 Val Met Met Phe Lys Lys Gly Ser Phe Glu Ile Gly Gly Thr Ile His  
 85                      90                      95  
 Pro Val Ala Ile Lys Tyr Asn Pro Gln Phe Gly Asp Ala Phe Trp Asn  
 100                      105                      110  
 Ser Ser Lys Tyr Asn Met Val Ser Tyr Leu Leu Arg Met Met Thr Ser  
 115                      120                      125  
 Trp Ala Ile Val Cys Asp Val Trp Tyr Met Pro Pro Met Thr Arg Glu  
 130                      135                      140  
 Glu Gly Glu Asp Ala Val Gln Phe Ala Asn Arg Val Lys Ser Ala Ile  
 145                      150                      155                      160  
 Ala Ile Gln Gly Gly Leu Thr Glu Leu Pro Trp Asp Gly Gly Leu Lys  
 165                      170                      175  
 Arg Ala Lys Val Lys Asp Ile Phe Lys Glu Glu Gln Gln Lys Asn Tyr  
 180                      185                      190  
 Ser Lys Met Ile Val Gly Asn Gly Ser Leu Ser  
 195                      200                      203

<210> 392  
 <211> 1637  
 <212> PRT  
 <213> Homo sapiens

<400> 392  
 Gln Leu Arg Gly Glu Ser Asp Arg Ser Lys Gln Pro Pro Pro Ala Ser  
 1                      5                      10                      15  
 Ser Pro Thr Lys Arg Lys Gly Arg Ser Arg Ala Leu Glu Ala Val Pro  
 20                      25                      30  
 Ala Pro Pro Ala Ser Gly Pro Arg Ala Pro Ala Lys Glu Ser Pro Pro  
 35                      40                      45  
 Lys Arg Val Pro Asp Pro Ser Pro Val Thr Lys Gly Thr Ala Ala Glu  
 50                      55                      60  
 Ser Gly Glu Glu Ala Ala Arg Ala Ile Pro Arg Glu Leu Pro Val Lys  
 65                      70                      75                      80  
 Ser Ser Ser Leu Leu Pro Glu Ile Lys Pro Glu His Lys Arg Gly Pro  
 85                      90                      95  
 Leu Pro Asn His Phe Asn Gly Arg Ala Glu Gly Gly Arg Ser Arg Glu  
 100                      105                      110

Leu Gly Arg Ala Ala Gly Ala Pro Gly Ala Ser Asp Ala Asp Gly Leu  
 115 120 125  
 Lys Pro Arg Asn His Phe Gly Val Gly Arg Ser Thr Val Thr Thr Lys  
 130 135 140  
 Val Thr Leu Pro Ala Lys Pro Lys His Val Glu Leu Asn Leu Lys Thr  
 145 150 155 160  
 Pro Lys Asn Leu Asp Ser Leu Gly Asn Glu His Asn Pro Phe Ser Gln  
 165 170 175  
 Pro Val His Lys Gly Asn Thr Ala Thr Lys Ile Ser Leu Phe Glu Asn  
 180 185 190  
 Lys Arg Thr Asn Ser Ser Pro Arg His Thr Asp Ile Arg Gly Pro Arg  
 195 200 205  
 Asn Thr Pro Ala Ser Ser Lys Thr Phe Val Gly Arg Ala Lys Leu Asn  
 210 215 220  
 Leu Ala Lys Lys Ala Lys Glu Met Glu Gln Pro Glu Lys Lys Val Met  
 225 230 235 240  
 Pro Asn Ser Pro Gln Asn Gly Val Leu Val Lys Glu Thr Ala Ile Glu  
 245 250 255  
 Thr Lys Val Thr Val Ser Glu Glu Glu Ile Leu Pro Ala Thr Arg Gly  
 260 265 270  
 Met Asn Gly Asp Ser Ser Glu Asn Gln Ala Leu Gly Pro Gln Pro Asn  
 275 280 285  
 Gln Asp Asp Lys Ala Asp Val Gln Thr Asp Ala Gly Cys Leu Ser Glu  
 290 295 300  
 Pro Val Ala Ser Ala Leu Ile Pro Val Lys Asp His Lys Leu Leu Glu  
 305 310 315 320  
 Lys Glu Asp Ser Glu Ala Ala Asp Ser Lys Ser Leu Val Leu Glu Asn  
 325 330 335  
 Val Thr Asp Thr Ala Gln Asp Ile Pro Thr Thr Val Asp Thr Lys Asp  
 340 345 350  
 Leu Pro Pro Thr Ala Met Pro Lys Pro Gln His Thr Phe Ser Asp Ser  
 355 360 365  
 Gln Ser Pro Ala Glu Ser Ser Pro Gly Pro Ser Leu Ser Leu Ser Ala  
 370 375 380  
 Pro Ala Pro Gly Asp Val Pro Lys Asp Thr Cys Val Gln Ser Pro Ile  
 385 390 395 400  
 Ser Ser Phe Pro Cys Thr Asp Leu Lys Val Ser Glu Asn His Lys Gly  
 405 410 415  
 Cys Val Leu Pro Val Ser Arg Gln Asn Asn Glu Lys Met Pro Leu Leu  
 420 425 430  
 Glu Leu Gly Gly Glu Thr Thr Pro Pro Leu Ser Thr Glu Arg Ser Pro  
 435 440 445  
 Glu Ala Val Gly Ser Glu Cys Pro Ser Arg Val Leu Val Gln Val Arg  
 450 455 460  
 Ser Phe Val Leu Pro Val Glu Ser Thr Gln Asp Val Ser Ser Gln Val  
 465 470 475 480  
 Ile Pro Glu Ser Ser Glu Val Arg Glu Val Gln Leu Pro Thr Cys His  
 485 490 495  
 Ser Asn Glu Pro Glu Val Val Ser Val Ala Ser Cys Ala Pro Pro Gln  
 500 505 510  
 Glu Glu Val Leu Gly Asn Glu His Ser His Cys Thr Ala Glu Leu Ala  
 515 520 525  
 Ala Lys Ser Gly Pro Gln Val Ile Pro Pro Ala Ser Glu Lys Thr Leu  
 530 535 540  
 Pro Ile Gln Ala Gln Ser Gln Gly Ser Arg Thr Pro Leu Met Ala Glu  
 545 550 555 560  
 Ser Ser Pro Thr Asn Ser Pro Ser Ser Gly Asn His Leu Ala Thr Pro  
 565 570 575  
 Gln Arg Pro Asp Gln Thr Val Thr Asn Gly Gln Asp Ser Pro Ala Ser  
 580 585 590  
 Leu Leu Asn Ile Ser Ala Gly Ser Asp Asp Ser Val Phe Asp Ser Ser  
 595 600 605  
 Ser Asp Met Glu Lys Phe Thr Glu Ile Ile Lys Gln Met Asp Ser Ala

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        610                615                620
Val Cys Met Pro Met Lys Arg Lys Lys Ala Arg Met Pro Asn Ser Pro
625                630                635                640
Ala Pro His Phe Ala Met Pro Pro Ile His Glu Asp His Leu Glu Lys
        645                650                655
Val Phe Asp Pro Lys Val Phe Thr Phe Gly Leu Gly Lys Lys Lys Glu
        660                665                670
Ser Gln Pro Glu Met Ser Pro Ala Leu His Leu Met Gln Asn Leu Asp
        675                680                685
Thr Lys Ser Lys Leu Arg Pro Lys Arg Ala Ser Ala Glu Gln Ser Val
        690                695                700
Leu Phe Lys Ser Leu His Thr Asn Thr Asn Gly Asn Ser Glu Pro Leu
705                710                715                720
Val Met Pro Glu Ile Asn Asp Lys Glu Asn Arg Asp Val Thr Asn Gly
        725                730                735
Gly Ile Lys Arg Ser Arg Leu Glu Lys Ser Ala Leu Phe Ser Ser Leu
        740                745                750
Leu Ser Ser Leu Pro Gln Asp Lys Ile Phe Ser Pro Ser Val Thr Ser
        755                760                765
Val Asn Thr Met Thr Thr Ala Phe Ser Thr Ser Gln Asn Gly Ser Leu
770                775                780
Ser Gln Ser Ser Val Ser Gln Pro Thr Thr Glu Gly Ala Pro Pro Cys
785                790                795                800
Gly Leu Asn Lys Glu Gln Ser Asn Leu Leu Pro Asp Asn Ser Leu Lys
        805                810                815
Val Phe Asn Phe Asn Ser Ser Ser Thr Ser His Ser Ser Leu Lys Ser
        820                825                830
Pro Ser His Met Glu Lys Tyr Pro Gln Lys Glu Lys Thr Lys Glu Asp
        835                840                845
Leu Asp Ser Arg Ser Asn Leu His Leu Pro Glu Thr Lys Phe Ser Glu
850                855                860
Leu Ser Lys Leu Lys Asn Asp Asp Met Glu Lys Ala Asn His Ile Glu
865                870                875                880
Ser Val Ile Lys Ser Asn Leu Pro Asn Cys Ala Asn Ser Asp Thr Asp
        885                890                895
Phe Met Gly Leu Phe Lys Ser Ser Arg Tyr Asp Pro Ser Ile Ser Phe
900                905                910
Ser Gly Met Ser Leu Ser Asp Thr Met Thr Leu Arg Gly Ser Val Gln
915                920                925
Asn Lys Leu Asn Pro Arg Pro Gly Lys Val Val Ile Tyr Ser Glu Pro
930                935                940
Asp Val Ser Glu Lys Cys Ile Glu Val Phe Ser Asp Ile Gln Asp Cys
945                950                955                960
Ser Ser Trp Ser Leu Ser Pro Val Ile Leu Ile Lys Val Val Arg Gly
        965                970                975
Cys Trp Ile Leu Tyr Glu Gln Pro Asn Phe Glu Gly His Ser Ile Pro
980                985                990
Leu Glu Glu Gly Glu Leu Glu Leu Ser Gly Leu Trp Gly Ile Glu Asp
995                1000                1005
Ile Leu Glu Arg His Glu Glu Ala Glu Ser Asp Lys Pro Val Val Ile
1010                1015                1020
Gly Ser Ile Arg His Val Val Gln Asp Tyr Arg Val Ser His Ile Asp
1025                1030                1035                1040
Leu Phe Thr Glu Pro Glu Gly Leu Gly Ile Leu Ser Ser Tyr Phe Asp
        1045                1050                1055
Asp Thr Glu Glu Met Gln Gly Phe Gly Val Met Gln Lys Thr Cys Ser
1060                1065                1070
Met Lys Val His Trp Gly Thr Trp Leu Ile Tyr Glu Glu Pro Gly Phe
1075                1080                1085
Gln Gly Val Pro Phe Ile Leu Glu Pro Gly Glu Tyr Pro Asp Leu Ser
1090                1095                1100
Phe Trp Asp Thr Glu Ala Ala Tyr Ile Gly Ser Met Arg Pro Leu Lys
1105                1110                1115                1120

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Met Gly Gly Arg Lys Val Glu Phe Pro Thr Asp Pro Lys Val Val Val  
 1125 1130 1135  
 Tyr Glu Lys Pro Phe Phe Glu Gly Lys Cys Val Glu Leu Glu Thr Gly  
 1140 1145 1150  
 Met Cys Ser Phe Val Met Glu Gly Gly Glu Thr Glu Glu Ala Thr Gly  
 1155 1160 1165  
 Asp Asp His Leu Pro Phe Thr Ser Val Gly Ser Met Lys Val Leu Arg  
 1170 1175 1180  
 Gly Ile Trp Val Ala Tyr Glu Lys Pro Gly Phe Thr Gly His Gln Tyr  
 1185 1190 1195 1200  
 Leu Leu Glu Glu Gly Glu Tyr Arg Asp Trp Lys Ala Trp Gly Gly Tyr  
 1205 1210 1215  
 Asn Gly Glu Leu Gln Ser Leu Arg Pro Ile Leu Gly Asp Phe Ser Asn  
 1220 1225 1230  
 Ala His Met Ile Met Tyr Ser Glu Lys Asn Phe Gly Ser Lys Gly Ser  
 1235 1240 1245  
 Ser Ile Asp Val Leu Gly Ile Val Ala Asn Leu Lys Glu Thr Gly Tyr  
 1250 1255 1260  
 Gly Val Lys Thr Gln Ser Ile Asn Val Leu Ser Gly Val Trp Val Ala  
 1265 1270 1275 1280  
 Tyr Glu Asn Pro Asp Phe Thr Gly Glu Gln Tyr Ile Leu Asp Lys Gly  
 1285 1290 1295  
 Phe Tyr Thr Ser Phe Glu Asp Trp Gly Gly Lys Asn Tyr Lys Ile Ser  
 1300 1305 1310  
 Ser Val Gln Pro Ile Cys Leu Asp Ser Phe Thr Gly Pro Arg Arg Arg  
 1315 1320 1325  
 Asn Gln Ile His Leu Phe Ser Glu Pro Gln Phe Gln Gly His Ser Gln  
 1330 1335 1340  
 Ser Phe Glu Glu Thr Thr Ser Gln Ile Asp Asp Ser Phe Ser Thr Lys  
 1345 1350 1355 1360  
 Ser Cys Arg Val Ser Gly Gly Ser Trp Val Val Tyr Asp Gly Glu Asn  
 1365 1370 1375  
 Phe Thr Gly Asn Gln Tyr Val Leu Glu Glu Gly His Tyr Pro Cys Leu  
 1380 1385 1390  
 Ser Ala Met Gly Cys Pro Pro Gly Ala Thr Phe Lys Ser Leu Arg Phe  
 1395 1400 1405  
 Ile Asp Val Glu Phe Ser Glu Pro Thr Ile Ile Leu Phe Glu Arg Glu  
 1410 1415 1420  
 Asp Phe Lys Gly Lys Lys Ile Glu Leu Asn Ala Glu Thr Val Asn Leu  
 1425 1430 1435 1440  
 Arg Ser Leu Gly Phe Asn Thr Gln Ile Arg Ser Val Gln Val Ile Gly  
 1445 1450 1455  
 Gly Ile Trp Val Thr Tyr Glu Tyr Gly Ser Tyr Arg Gly Arg Gln Phe  
 1460 1465 1470  
 Leu Leu Ser Pro Ala Glu Val Pro Asn Trp Tyr Glu Phe Ser Gly Cys  
 1475 1480 1485  
 Arg Gln Ile Gly Ser Leu Arg Pro Phe Val Gln Lys Arg Ile Tyr Phe  
 1490 1495 1500  
 Arg Leu Arg Asn Lys Ala Thr Gly Leu Phe Met Ser Thr Asn Gly Asn  
 1505 1510 1515 1520  
 Leu Glu Asp Leu Lys Leu Leu Arg Ile Gln Val Met Glu Asp Val Gly  
 1525 1530 1535  
 Ala Asp Asp Gln Ile Trp Ile Tyr Gln Glu Gly Cys Ile Lys Cys Arg  
 1540 1545 1550  
 Ile Ala Glu Asp Cys Cys Leu Thr Ile Val Gly Ser Leu Val Thr Ser  
 1555 1560 1565  
 Gly Ser Lys Leu Gly Leu Ala Leu Asp Gln Asn Ala Asp Ser Gln Phe  
 1570 1575 1580  
 Trp Ser Leu Lys Ser Asp Gly Arg Ile Tyr Ser Lys Leu Lys Pro Asn  
 1585 1590 1595 1600  
 Leu Val Leu Asp Ile Lys Gly Gly Thr Gln Tyr Asp Gln Asn His Ile  
 1605 1610 1615  
 Ile Leu Asn Thr Val Ser Lys Glu Lys Phe Thr Gln Val Trp Glu Ala

1620 1625 1630  
Met Val Leu Tyr Thr  
1635 1637

<210> 393  
<211> 102  
<212> PRT  
<213> Homo sapiens

<400> 393  
Leu Phe Ile Gly Gly Pro Ser Asn Met Ile Arg Ser Ala Ile Ser Ala  
1 5 10 15  
Asp Leu Gly Arg Gln Glu Leu Ile Gln Arg Ser Ser Glu Ala Leu Ala  
20 25 30  
Thr Val Thr Gly Ile Val Asp Gly Ser Gly Ser Ile Gly Ala Ala Val  
35 40 45  
Gly Gln Tyr Leu Val Ser Leu Ile Arg Asp Lys Leu Gly Trp Met Trp  
50 55 60  
Val Phe Tyr Phe Phe Ile Leu Met Thr Ser Cys Thr Ile Val Phe Ile  
65 70 75 80  
Ser Pro Leu Ile Val Arg Glu Ile Phe Ser Leu Val Leu Arg Arg Gln  
85 90 95  
Ala His Ile Leu Arg Glu  
100 102

<210> 394  
<211> 370  
<212> PRT  
<213> Homo sapiens

<400> 394  
Arg Arg Gln Leu Gly Val Ala Leu Ile Pro Ser His Arg Met Asp Tyr  
1 5 10 15  
Lys Ser Ser Leu Ile Gln Asp Gly Asn Pro Met Glu Asn Leu Glu Lys  
20 25 30  
Gln Leu Ile Cys Pro Ile Cys Leu Glu Met Phe Thr Lys Pro Val Val  
35 40 45  
Ile Leu Pro Cys Gln His Asn Leu Cys Arg Lys Cys Ala Asn Asp Ile  
50 55 60  
Phe Gln Ala Ala Asn Pro Tyr Trp Thr Ser Arg Gly Ser Ser Val Ser  
65 70 75 80  
Met Ser Gly Gly Arg Phe Arg Cys Pro Thr Cys Arg His Glu Val Ile  
85 90 95  
Met Asp Arg His Gly Val Tyr Gly Leu Gln Arg Asn Leu Leu Val Glu  
100 105 110  
Asn Ile Ile Asp Ile Tyr Lys Gln Glu Cys Ser Ser Arg Pro Leu Gln  
115 120 125  
Lys Gly Ser His Pro Met Cys Lys Glu His Glu Asp Glu Lys Ile Asn  
130 135 140  
Ile Tyr Cys Leu Thr Cys Glu Val Pro Thr Cys Ser Met Cys Lys Val  
145 150 155 160  
Phe Gly Ile His Lys Ala Cys Glu Val Ala Pro Leu Gln Ser Val Phe  
165 170 175  
Gln Gly Gln Lys Thr Glu Leu Asn Asn Cys Ile Ser Met Leu Val Ala  
180 185 190  
Gly Asn Asp Arg Val Gln Thr Ile Ile Thr Gln Leu Glu Asp Ser Arg  
195 200 205  
Arg Val Thr Lys Glu Asn Ser His Gln Val Lys Glu Glu Leu Ser Gln  
210 215 220

Lys Phe Asp Thr Leu Tyr Ala Ile Leu Asp Glu Lys Lys Ser Glu Leu  
 225 230 235 240  
 Leu Gln Arg Ile Thr Gln Glu Gln Glu Lys Lys Leu Ser Phe Ile Glu  
 245 250 255  
 Ala Leu Ile Gln Gln Tyr Gln Glu Gln Leu Asp Lys Ser Thr Lys Leu  
 260 265 270  
 Val Glu Thr Ala Ile Gln Ser Leu Asp Glu Pro Gly Gly Ala Thr Phe  
 275 280 285  
 Leu Leu Thr Ala Lys Gln Leu Ile Lys Ser Ile Val Glu Ala Ser Lys  
 290 295 300  
 Gly Cys Gln Leu Gly Lys Thr Glu Gln Gly Phe Glu Asn Met Asp Phe  
 305 310 315 320  
 Phe Thr Leu Asp Leu Glu His Ile Ala Asp Ala Leu Arg Ala Ile Asp  
 325 330 335  
 Phe Gly Thr Asp Glu Glu Glu Glu Glu Phe Ile Glu Glu Glu Asp Gln  
 340 345 350  
 Glu Glu Glu Glu Ser Thr Glu Gly Lys Glu Glu Gly His Gln Leu Gly  
 355 360 365  
 Ala Gly  
 370

<210> 395  
 <211> 236  
 <212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(231)  
 <223> Xaa = any amino acid or nothing

<400> 395  
 Val Lys Thr His Phe Thr Cys Lys Asp Ala Xaa Arg Leu Lys Val Lys  
 1 5 10 15  
 Glu Xaa Xaa Asn Ile Phe His Ala Asn Glu Lys Gln Lys Gln Ala Arg  
 20 25 30  
 Val Ala Ile Val Val Ser Gly Lys Ile Asp Phe Lys Asn Gly Lys Asn  
 35 40 45  
 Lys Asn Asn Asn Glu Asp Asp His Tyr Ile Met Thr Lys Arg Xaa Ile  
 50 55 60  
 Gln Gln Glu Asp Ile Pro Val Leu Asn Ile Tyr Ala Tyr Ala Ser Thr  
 65 70 75 80  
 Gly Ala Gln Arg Tyr Ile Lys Glu Ile Leu Phe Asp Leu Lys Gly Glu  
 85 90 95  
 Ile Asp Ser Asn Thr Ile Met Val Gly Asp Leu Asn Pro Leu Ser Ala  
 100 105 110  
 Ser Asp Arg Ser Cys Arg Gln Lys Ile Asn Met Asp Xaa Asn Cys Ala  
 115 120 125  
 Leu Asp Gln Ile Gly Leu Thr Asp Ile Tyr Arg Thr Phe Tyr Leu Thr  
 130 135 140  
 Ala Gly Glu Cys Thr Phe Phe Leu Ser Ala His Val Thr Phe Ser Arg  
 145 150 155 160  
 Ile Asp His Val Leu Gly His Lys Thr Ser Leu Asn Lys Ile Leu Lys  
 165 170 175  
 Ile Glu Ile Ile Ser Ser Ile Phe Leu Asp His Lys Gly Ile Lys Leu  
 180 185 190  
 Glu Phe Asn Asn Lys Asn Asn Phe Gly Ser Cys Thr Asn Thr Trp Lys  
 195 200 205  
 Val Asn Lys Met Leu Met Thr Asn Tyr Trp Val Ser Glu Glu Ile Met  
 210 215 220  
 Lys Glu Ile Lys Lys Lys Lys  
 225 230 231



<210> 396  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<400> 396  
 Tyr Gly Cys Glu Lys Thr Thr Glu Gly Thr Asp Gly Val Asn Phe Tyr  
   1                  5                  10                  15  
 Asn Ile Leu Thr Lys Ser Thr Pro Thr Ser Thr Met Glu Ser Ser Leu  
           20                  25                  30  
 Glu Phe Thr Gln Ser His Leu Val Cys Leu Cys Gln Arg His Val Arg  
           35                  40                  45  
 His Leu Gln Arg Asp Ala Leu Ser Gln Leu Met Asn Gly Pro Ile Arg  
           50                  55                  60  
 Lys Lys Leu Lys Ile Ile Pro Glu Asp Gln Ser Trp Gly Gly Gln Ala  
   65                  70                  75                  80  
 Thr Asn Val Phe Val Asn Met Glu Glu Asp Phe Met Lys Pro Val Ile  
                   85                  90                  95  
 Ser Ile Val Asp Glu Leu Leu Glu Ala Gly Ile Asn Val Thr Val Tyr  
                   100                  105                  110  
 Asn Gly Gln Leu Asp Leu Ile Val Asp Thr Met Gly Gln Glu Ala Trp  
           115                  120                  125  
 Val Arg Lys Leu Lys Trp Pro Glu Leu Pro Lys Phe Ser Gln Leu Lys  
   130                  135                  140  
 Trp Lys Ala Leu Tyr Ser Asp Pro Lys Ser Leu Glu Thr Ser Ala Phe  
   145                  150                  155                  160  
 Val Lys Ser Tyr Lys Asn Leu Ala Phe Tyr Trp Ile Leu Lys Ala Gly  
                   165                  170                  175  
 His Met Val Pro Ser Asp Gln Gly Asp Met Ala Leu Lys Met Met Arg  
                   180                  185                  190  
 Leu Val Thr Gln Gln Glu  
           195                  198

<210> 397  
 <211> 190  
 <212> PRT  
 <213> Homo sapiens

<400> 397  
 Gly Ser Thr His Ala Ser Ala Asn Ile Cys Glu Val Cys Asn Lys Trp  
   1                  5                  10                  15  
 Gly Arg Leu Phe Cys Cys Asp Thr Cys Pro Arg Ser Phe His Glu His  
           20                  25                  30  
 Cys His Ile Pro Ser Val Glu Ala Asn Lys Asn Pro Trp Ser Cys Ile  
           35                  40                  45  
 Phe Cys Arg Ile Lys Thr Ile Gln Glu Arg Cys Pro Glu Ser Gln Ser  
   50                  55                  60  
 Gly His Gln Glu Ser Glu Val Leu Met Arg Gln Met Leu Pro Glu Glu  
   65                  70                  75                  80  
 Gln Leu Lys Cys Glu Phe Leu Leu Leu Lys Val Tyr Cys Asp Ser Lys  
                   85                  90                  95  
 Ser Cys Phe Phe Ala Ser Glu Pro Tyr Asn Arg Glu Gly Ser Gln  
                   100                  105                  110  
 Gly Pro Gln Lys Pro Met Trp Leu Asn Lys Val Lys Thr Ser Leu Asn  
           115                  120                  125  
 Glu Gln Met Tyr Thr Arg Val Glu Gly Phe Val Gln Asp Met Arg Leu  
   130                  135                  140  
 Ile Phe His Asn His Lys Glu Phe Tyr Arg Glu Asp Lys Phe Thr Arg

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<210> 398
<211> 173
<212> PRT
<213> Homo sapiens
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<210> 399
<211> 550
<212> PRT
<213> Homo sapiens
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285

Ala Lys Gly Leu Pro Asp Met Asp Ser Ser Ile Leu Ile His His Asn  
 145 150 155 160  
 Gly Gly Ile Pro Ala Asn Lys Lys Leu Ser Thr Thr Leu Pro Glu Ile  
 165 170 175  
 Glu Tyr Arg Glu Lys Gly Lys Glu Lys Asp Lys Asp Ala Lys Lys His  
 180 185 190  
 Asn Leu Gly Ile Asn Asn Asn Asn Ile Leu Gln Pro Val Asp Ser Lys  
 195 200 205  
 Ile Gln Glu Ile Glu Tyr Met Glu Asn His Ile Asn Ser Lys Arg Leu  
 210 215 220  
 Asn Asn Asp Leu Val Gly Ser Thr Glu Asn Leu Leu Lys Glu Asp Ser  
 225 230 235 240  
 Cys Thr Ala Ser Ser Lys Asn Tyr Lys Asn Ala Ser Gly Val Val Asn  
 245 250 255  
 Ser Ser Pro Arg Ser His Ser Ala Thr Asn Gly Ser Ile Pro Ser Ser  
 260 265 270  
 Ser Ser Lys Asn Glu Lys Lys Gln Lys Cys Thr Ser Lys Ser Pro Ser  
 275 280 285  
 Thr His Lys Asp Leu Met Glu Asn Cys Ile Pro Asn Asn Gln Leu Ser  
 290 295 300  
 Lys Pro Asp Ala Leu Val Arg Leu Glu Gln Asp Ile Lys Lys Leu Lys  
 305 310 315 320  
 Ala Asp Leu Gln Ala Ser Arg Gln Val Glu Gln Glu Leu Arg Ser Gln  
 325 330 335  
 Ile Ser Ser Leu Ser Ser Thr Glu Arg Gly Ile Arg Ser Glu Met Gly  
 340 345 350  
 Gln Leu Arg Gln Glu Asn Glu Leu Gln Asn Lys Leu His Asn Ala  
 355 360 365  
 Val Gln Met Lys Gln Lys Asp Lys Gln Asn Ile Ser Gln Leu Glu Lys  
 370 375 380  
 Lys Leu Lys Ala Glu Gln Glu Ala Arg Ser Phe Val Glu Lys Gln Leu  
 385 390 395 400  
 Met Glu Glu Lys Lys Arg Lys Lys Leu Glu Glu Ala Thr Ala Ala Arg  
 405 410 415  
 Ala Val Ala Phe Ala Ala Ala Ser Arg Gly Glu Cys Thr Glu Thr Leu  
 420 425 430  
 Arg Asn Arg Ile Arg Glu Leu Glu Ala Glu Gly Lys Lys Leu Thr Met  
 435 440 445  
 Asp Met Lys Val Lys Glu Asp Gln Ile Arg Glu Leu Glu Lys Val  
 450 455 460  
 Gln Glu Leu Arg Lys Tyr Lys Glu Asn Glu Lys Asp Thr Glu Val Leu  
 465 470 475 480  
 Met Ser Ala Leu Ser Ala Met Gln Asp Lys Thr Gln His Leu Glu Asn  
 485 490 495  
 Ser Leu Ser Ala Glu Thr Arg Ile Lys Leu Asp Leu Phe Ser Ala Leu  
 500 505 510  
 Gly Asp Ala Lys Arg Gln Leu Glu Ile Ala Gln Gly Gln Ile Leu Gln  
 515 520 525  
 Lys Asp Gln Glu Ile Lys Asp Leu Lys Gln Lys Ile Ala Glu Val Met  
 530 535 540  
 Gly Arg His Ala Gln Pro  
 545 550

&lt;210&gt; 400

&lt;211&gt; 488

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 400

Ile Arg Ile Ser Arg Val Asp Asp Phe Val Lys Leu Ile Arg Leu Ser  
 1 5 10 15

Gln Ile Lys Glu Lys Met Ala Arg Glu Lys Leu Glu Glu Ile Asp Trp  
 20 25 30  
 Val Thr Phe Gly Val Ile Leu Lys Lys Val Thr Pro Gln Ser Val Asn  
 35 40 45  
 Ser Gly Lys Thr Phe Ser Ile Trp Lys Leu Asn Asp Leu Arg Asp Leu  
 50 55 60  
 Thr Gln Cys Val Ser Leu Phe Leu Phe Gly Glu Val His Lys Ala Leu  
 65 70 75 80  
 Trp Lys Thr Glu Gln Gly Thr Val Val Gly Ile Leu Asn Ala Asn Pro  
 85 90 95  
 Met Lys Pro Lys Asp Gly Ser Glu Glu Val Cys Leu Ser Ile Asp His  
 100 105 110  
 Pro Gln Lys Val Leu Ile Met Gly Glu Ala Leu Asp Leu Gly Thr Cys  
 115 120 125  
 Lys Ala Lys Lys Lys Asn Gly Glu Pro Cys Thr Gln Thr Val Asn Leu  
 130 135 140  
 Arg Asp Cys Glu Tyr Cys Gln Tyr His Val Gln Ala Gln Tyr Lys Lys  
 145 150 155 160  
 Leu Ser Ala Lys Arg Ala Asp Leu Gln Ser Thr Phe Ser Gly Gly Arg  
 165 170 175  
 Ile Pro Lys Lys Phe Ala Arg Arg Gly Thr Ser Leu Lys Glu Arg Leu  
 180 185 190  
 Cys Gln Asp Gly Phe Tyr Tyr Gly Gly Val Ser Ser Ala Ser Tyr Ala  
 195 200 205  
 Ala Ser Ile Ala Ala Ala Val Ala Pro Lys Lys Lys Ile Gln Thr Thr  
 210 215 220  
 Leu Ser Asn Leu Val Val Lys Gly Thr Asn Leu Ile Ile Gln Glu Thr  
 225 230 235 240  
 Arg Gln Lys Leu Gly Ile Pro Gln Lys Ser Leu Ser Cys Ser Glu Glu  
 245 250 255  
 Phe Lys Glu Leu Met Asp Leu Pro Thr Cys Gly Ala Arg Asn Leu Lys  
 260 265 270  
 Gln His Leu Ala Lys Ala Thr Ala Ser Gly Ile Met Gly Ser Pro Lys  
 275 280 285  
 Pro Ala Ile Lys Ser Ile Ser Ala Ser Ala Leu Leu Lys Gln Gln Lys  
 290 295 300  
 Gln Arg Met Leu Glu Met Arg Arg Arg Lys Ser Glu Glu Ile Gln Lys  
 305 310 315 320  
 Arg Phe Leu Gln Ser Ser Ser Glu Val Glu Ser Pro Ala Val Pro Ser  
 325 330 335  
 Ser Ser Arg Gln Pro Pro Ala Gln Pro Pro Arg Thr Gly Ser Glu Phe  
 340 345 350  
 Pro Arg Leu Glu Gly Ala Pro Ala Thr Met Thr Pro Lys Leu Gly Arg  
 355 360 365  
 Gly Val Leu Glu Gly Asp Asp Val Leu Phe Tyr Asp Glu Ser Pro Pro  
 370 375 380  
 Pro Arg Pro Lys Leu Ser Ala Leu Ala Glu Ala Lys Lys Leu Ala Ala  
 385 390 395 400  
 Ile Thr Lys Leu Arg Ala Lys Gly Gln Val Leu Thr Lys Thr Asn Pro  
 405 410 415  
 Asn Ser Ile Lys Lys Lys Gln Lys Asp Pro Gln Asp Ile Leu Glu Val  
 420 425 430  
 Lys Glu Arg Val Glu Lys Asn Thr Met Phe Ser Ser Gln Ala Glu Asp  
 435 440 445  
 Glu Leu Glu Pro Ala Arg Lys Lys Arg Arg Glu Gln Leu Ala Tyr Leu  
 450 455 460  
 Glu Phe Glu Glu Phe Gln Lys Ile Leu Lys Ala Lys Ser Lys His Thr  
 465 470 475 480  
 Gly His Pro Glu Arg Gly Arg Gly  
 485 488

<211> 206  
 <212> PRT  
 <213> Homo sapiens

<400> 401  
 Phe Leu Gln Met Arg Gln His Arg Asp Pro His Ile Leu Gln Lys Pro  
 1 5 10 15  
 Phe Asn Val Thr Glu Thr Arg Cys Leu Pro Lys Pro Ser Arg Thr Thr  
 20 25 30  
 Ser Trp Cys Lys Ala Ile Pro Pro Asp Ser Glu Lys Ser Ile Ser Ile  
 35 40 45  
 Cys Asp Asn Leu Ser Glu Leu Leu Met Ala Met Gln Asp Glu Leu Asp  
 50 55 60  
 Gln Met Ser Met Glu His Gln Glu Leu Leu Lys Gln Met Lys Glu Thr  
 65 70 75 80  
 Glu Ser His Ser Val Cys Asp Asp Ile Glu Cys Glu Leu Glu Cys Leu  
 85 90 95  
 Leu Lys Lys Met Glu Ile Lys Gly Glu Gln Ile Ser Lys Leu Lys Lys  
 100 105 110  
 His Gln Asp Ser Val Cys Lys Leu Gln Gln Lys Val Gln Asn Ser Lys  
 115 120 125  
 Met Ser Glu Ala Ser Gly Ile Gln Gln Glu Asp Ser Tyr Pro Lys Gly  
 130 135 140  
 Ser Lys Asn Ile Lys Asn Ser Pro Arg Lys Cys Leu Thr Asp Thr Asn  
 145 150 155 160  
 Leu Phe Gln Lys Asn Ser Ser Phe His Pro Ile Arg Val His Asn Leu  
 165 170 175  
 Gln Met Lys Leu Arg Arg Asp Asp Ile Met Trp Glu Pro Val Thr Lys  
 180 185 190  
 Gln Gln Asn Cys His Leu Asn Gly Leu Trp Ser Val Arg Pro  
 195 200 205 206

<210> 402  
 <211> 189  
 <212> PRT  
 <213> Homo sapiens

<221> misc\_feature  
 <222> (1)...(188)  
 <223> Xaa = any amino acid or nothing

<400> 402  
 Arg Pro Gly Phe Pro Trp Gln Glu Ile Pro Lys Val Trp Ser Gly Leu  
 1 5 10 15  
 Ser Leu Ser Leu Val Ser Gln His Met Lys Xaa Lys Ser Val Gln Leu  
 20 25 30  
 Leu Phe Arg Leu Leu Arg Gly Asp Ile Ala Thr Glu Gln Val Asp Val  
 35 40 45  
 Ile Val Asn Ser Thr Ala Arg Thr Phe Asn Arg Lys Ser Gly Val Ser  
 50 55 60  
 Arg Ala Ile Leu Glu Gly Ala Gly Gln Ala Val Glu Ser Glu Cys Ala  
 65 70 75 80  
 Val Leu Ala Ala Gln Pro His Arg Asp Phe Ile Ile Thr Pro Gly Gly  
 85 90 95  
 Cys Leu Lys Cys Lys Ile Ile Ile His Val Pro Gly Gly Lys Asp Val  
 100 105 110  
 Arg Lys Thr Val Thr Ser Val Leu Glu Glu Cys Glu Gln Arg Lys Tyr  
 115 120 125  
 Thr Ser Val Ser Leu Pro Ala Ile Gly Thr Gly Asn Ala Gly Lys Asn  
 130 135 140

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Pro Ile Thr Val Ala Asp Asn Ile Ile Asp Ala Ile Val Asp Phe Ser
145             150             155             160
Ser Gln His Ser Thr Pro Ser Leu Lys Thr Val Lys Val Val Ile Phe
             165             170             175
Gln Pro Glu Leu Leu Asn Ile Phe Tyr Asp Ser Met
             180             185             188

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<210> 403
<211> 123
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(123)
<223> Xaa = any amino acid or nothing

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<400> 403
Trp Glu Leu Leu Thr Ala Ile Trp Thr Pro Leu Cys Gly Phe Ser Ser
 1             5             10             15
Ser Trp Lys Gly Ser Met Arg Leu Asp Arg Cys Glu Ala Pro Val His
             20             25             30
Pro Glu Lys Cys Pro Pro Asp Leu Arg Ala Gly Met Ile Ala Leu Ser
             35             40             45
Pro Val Ser Leu Tyr Ile Ser Ala Trp Phe Ser Phe Leu Phe Ser Val
             50             55             60
Pro Arg Phe Ile Val Leu Cys Arg Phe Val Leu Ser Pro Cys Arg Pro
             65             70             75             80
His Leu Phe Ile Phe Val Xaa Gln Ile Leu Leu Glu Ala Tyr Xaa Ile
             85             90             95
Pro Phe Thr Val Ile Gly Gln Gly Thr Trp Trp Xaa Ala Gly Gln Asn
             100             105             110
Ser Cys Pro His Thr Lys Ser Ser Thr Arg Glu
             115             120             123

```

```

<210> 404
<211> 431
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(427)
<223> Xaa = any amino acid or nothing

```

```

<400> 404
Lys Leu Ser Ala Glu Ser Tyr Lys Glu Thr Gln Met Val Lys Ile Lys
 1             5             10             15
Glu Glu Pro Met Glu Val Asp Ile Gln Asp Ser His Val Ser Ile Ser
             20             25             30
Pro Ser Arg Asn Val Gly Tyr Ser Thr Leu Ile Gly Arg Glu Lys Thr
             35             40             45
Glu Pro Leu Gln Lys Met Pro Glu Gly Arg Val Pro Pro Glu Arg Asn
             50             55             60
Leu Phe Ser Gln Asp Ile Ser Val Lys Met Ala Ser Glu Leu Leu Phe
             65             70             75             80
Gln Leu Ser Glu Lys Val Ser Lys Glu His Asn His Thr Lys Glu Asn
             85             90             95
Thr Ile Arg Thr Thr Thr Ser Pro Phe Phe Ser Glu Asp Thr Phe Arg
             100             105             110
Gln Ser Pro Phe Thr Ser Asn Ser Lys Glu Leu Leu Pro Ser Asp Ser

```

```

      115              120              125
Val Leu His Gly Arg Ile Ser Ala Pro Glu Thr Glu Lys Ile Val Leu
      130              135              140
Glu Ala Gly Asn Gly Leu Pro Ser Trp Lys Phe Asn Asp Gln Leu Phe
      145              150              155              160
Pro Cys Asp Val Cys Gly Lys Val Phe Gly Arg Gln Gln Thr Leu Ser
      165              170              175
Arg His Leu Ser Leu His Thr Glu Glu Arg Lys Tyr Lys Cys His Leu
      180              185              190
Cys Pro Tyr Ala Ala Lys Cys Arg Ala Asn Leu Asn Gln His Leu Thr
      195              200              205
Val His Cys Arg Glu Ala Gly Glu Tyr Arg His Arg Gly His Cys Gln
      210              215              220
Arg Arg His Leu Xaa Arg His Asp Gly Lys Lys His Pro Tyr Tyr Tyr
      225              230              235              240
Ser Cys His Val Cys Gly Phe Glu Thr Glu Leu Asn Val Gln Phe Val
      245              250              255
Ser His Met Ser Leu His Val Asp Lys Glu Gln Trp Met Phe Ser Ile
      260              265              270
Cys Cys Thr Ala Cys Asp Phe Val Thr Met Glu Glu Ala Glu Ile Lys
      275              280              285
Thr His Ile Gly Thr Lys His Thr Gly Glu Asp Arg Lys Thr Pro Ser
      290              295              300
Glu Ser Asn Ser Pro Ser Ser Ser Ser Leu Ser Ala Arg Val Ile Gln
      305              310              315              320
Pro Thr Ala Lys Met Ile Gln Met Ala Pro Arg Lys Thr Arg Ala Gly
      325              330              335
Thr Ile Cys Trp Ser Ser Leu Ser Cys Leu Val Ser Gln Pro Ser Leu
      340              345              350
Asn Ser Glu Glu Lys Pro Glu Lys Gly Phe Glu Cys Val Phe Cys Asn
      355              360              365
Phe Val Cys Lys Thr Lys Asn Met Phe Glu Arg His Leu Gln Ile His
      370              375              380
Leu Ile Thr Arg Met Phe Glu Cys Asp Val Cys His Lys Phe Met Lys
      385              390              395              400
Thr Pro Glu Gln Leu Leu Glu His Lys Lys Cys His Thr Val Pro Thr
      405              410              415
Gly Gly Leu Asn Leu Cys Ser Arg Met Thr Lys
      420              425              427

```

<210> 405  
 <211> 68  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 405
Arg Gln Cys Leu Thr Leu Leu Pro Arg Leu Glu Cys Gly Gly Met Ile
      1              5              10              15
Arg Thr Asp Cys Asn Leu Glu Leu Met Gly Ser Ser Asp Pro Pro Ala
      20              25              30
Leu Ala Ser Gln Asn Pro Gly Ile Thr Asp Val Ser His His Thr Gly
      35              40              45
Gln Ile Leu Thr Ser Leu Leu Leu Lys Tyr Lys Cys Leu Ile Cys Arg
      50              55              60
His Ile Phe
      65              67

```

<210> 406  
 <211> 588  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 406

Ala Ala Ser Thr Arg Thr Met Gly Ser Arg His Phe Glu Gly Ile Tyr  
 1 5 10 15  
 Asp His Val Gly His Phe Gly Arg Phe Gln Arg Val Leu Tyr Phe Ile  
 20 25 30  
 Cys Ala Phe Gln Asn Ile Ser Cys Gly Ile His Tyr Leu Ala Ser Val  
 35 40 45  
 Phe Met Gly Val Thr Pro His His Val Cys Arg Pro Pro Gly Asn Val  
 50 55 60  
 Ser Gln Val Val Phe His Asn His Ser Asn Trp Ser Leu Glu Asp Thr  
 65 70 75 80  
 Gly Ala Leu Leu Ser Ser Gly Gln Lys Asp Tyr Val Thr Val Gln Leu  
 85 90 95  
 Gln Asn Gly Glu Ile Trp Glu Leu Ser Arg Cys Ser Arg Asn Lys Arg  
 100 105 110  
 Glu Asn Thr Ser Ser Leu Gly Tyr Glu Tyr Thr Gly Ser Lys Lys Glu  
 115 120 125  
 Phe Pro Cys Val Asp Gly Tyr Ile Tyr Asp Gln Asn Thr Trp Lys Ser  
 130 135 140  
 Thr Ala Val Thr Gln Trp Asn Leu Val Cys Asp Arg Lys Trp Leu Ala  
 145 150 155 160  
 Met Leu Ile Gln Pro Leu Phe Met Phe Gly Val Leu Leu Gly Ser Val  
 165 170 175  
 Thr Phe Gly Tyr Phe Ser Asp Arg Leu Gly Arg Arg Val Val Leu Trp  
 180 185 190  
 Ala Thr Ser Ser Ser Met Phe Leu Phe Gly Ile Ala Ala Ala Phe Ala  
 195 200 205  
 Val Asp Tyr Tyr Thr Phe Met Ala Ala Arg Phe Phe Leu Ala Met Val  
 210 215 220  
 Ala Ser Gly Tyr Leu Val Val Gly Phe Val Tyr Val Met Glu Phe Ile  
 225 230 235 240  
 Gly Met Lys Ser Arg Thr Trp Ala Ser Val His Leu His Ser Phe Phe  
 245 250 255  
 Ala Val Gly Thr Leu Leu Val Ala Leu Thr Gly Tyr Leu Val Arg Thr  
 260 265 270  
 Trp Trp Leu Tyr Gln Met Ile Leu Ser Thr Val Thr Val Pro Phe Ile  
 275 280 285  
 Leu Cys Cys Trp Val Leu Pro Glu Thr Pro Phe Trp Leu Leu Ser Glu  
 290 295 300  
 Gly Arg Tyr Glu Glu Ala Gln Lys Ile Val Asp Ile Met Ala Lys Trp  
 305 310 315 320  
 Asn Arg Ala Ser Ser Cys Lys Leu Ser Glu Leu Leu Ser Leu Asp Leu  
 325 330 335  
 Gln Gly Pro Val Ser Asn Ser Pro Thr Glu Val Gln Lys His Asn Leu  
 340 345 350  
 Ser Tyr Leu Phe Tyr Asn Trp Ser Ile Thr Lys Arg Thr Leu Thr Val  
 355 360 365  
 Trp Leu Ile Trp Phe Thr Gly Ser Leu Gly Phe Tyr Ser Phe Ser Leu  
 370 375 380  
 Asn Ser Val Asn Leu Gly Gly Asn Glu Tyr Leu Asn Leu Phe Leu Leu  
 385 390 395 400  
 Gly Val Val Glu Ile Pro Ala Tyr Thr Phe Val Cys Ile Ala Met Asp  
 405 410 415  
 Lys Val Gly Arg Arg Thr Val Leu Ala Tyr Ser Leu Phe Cys Ser Ala  
 420 425 430  
 Leu Ala Cys Gly Val Val Met Val Ile Pro Gln Lys His Tyr Ile Leu  
 435 440 445  
 Gly Val Val Thr Ala Met Val Gly Lys Ile Leu Pro Ile Gly Ala Ala  
 450 455 460  
 Phe Gly Leu Ile Tyr Leu Tyr Thr Ala Glu Leu Tyr Pro Thr Ile Val



```
<210> 407
<211> 986
<212> PRT
<213> Homo sapiens
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292

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305          310          315          320
Thr Pro Gln Ser Arg Ile Gln Asn Ala Ala Lys Arg Ser Pro Ala Thr
          325          330          335
Tyr Gly His Ser Gln Lys Lys His Lys Cys Ser Val Tyr Tyr Ser Lys
          340          345          350
His Lys Thr Ser Thr Ala Ala Ala Ser Ser Thr Ser Thr Thr Glu
          355          360          365
Glu Lys Gln Thr Ser Pro Leu Gly Ser Ser Leu Pro Ala Ala Lys Glu
          370          375          380
Asp Ile Cys Thr Asp Ala Met Arg Glu Asn Trp Ile Ser Leu Arg Tyr
385          390          395          400
Ala Ser Gly Ile Asn Val Asn Leu Gln Lys Asn Leu Thr Leu Pro Lys
          405          410          415
Asn Leu Leu Asn Lys Glu Glu Asn Thr Leu Lys Asn Thr Ile Val Phe
          420          425          430
Ser Asn Pro Ser Ser Glu Cys Ser Met Lys Glu Gly Ile Gln Thr Cys
          435          440          445
Met Phe Pro Lys Glu Thr Asp Ile Lys Thr Ser Glu Asn Thr Ala Glu
          450          455          460
Phe Lys Glu Arg Glu Leu Cys Pro Leu Lys Thr Ser Lys Lys Leu Pro
465          470          475          480
Glu Asn His Leu Pro Arg Asn Ser Pro Gln Tyr His Gln Pro Asp Leu
          485          490          495
Pro Glu Ile Ser Arg Lys Asn Asn Gly Asn Asn Gln Gln Val Pro Val
          500          505          510
Lys Asn Glu Val Asp His Cys Glu Asn Leu Lys Lys Val Asp Thr Lys
          515          520          525
Pro Ser Ser Glu Lys Lys Ile His Lys Thr Ser Arg Glu Asp Met Phe
          530          535          540
Ser Glu Lys Gln Asp Ile Pro Phe Val Glu Gln Glu Asp Pro Tyr Arg
545          550          555          560
Lys Lys Lys Leu Gln Glu Lys Arg Glu Gly Asn Leu Gln Asn Leu Asn
          565          570          575
Trp Ser Lys Ser Arg Thr Cys Arg Lys Asn Lys Lys Arg Gly Val Ala
          580          585          590
Pro Val Ser Arg Pro Pro Glu Gln Ser Asp Leu Lys Leu Val Cys Ser
          595          600          605
Asp Phe Glu Arg Ser Glu Leu Ser Ser Asp Ile Asn Val Arg Ser Trp
          610          615          620
Cys Ile Gln Glu Ser Thr Arg Glu Val Cys Lys Ala Asp Ala Glu Ile
625          630          635          640
Ala Ser Ser Leu Pro Ala Ala Gln Arg Glu Ala Glu Gly Tyr Tyr Gln
          645          650          655
Lys Pro Glu Lys Lys Cys Val Asp Lys Phe Cys Ser Asp Ser Ser Ser
          660          665          670
Asp Cys Gly Ser Ser Ser Gly Ser Val Arg Ala Ser Arg Gly Ser Trp
          675          680          685
Gly Ser Trp Ser Ser Thr Ser Ser Ser Asp Gly Asp Lys Lys Pro Met
          690          695          700
Val Asp Ala Gln His Phe Leu Pro Ala Gly Asp Ser Val Ser Gln Asn
705          710          715          720
Asp Phe Pro Ser Glu Ala Pro Ile Ser Leu Asn Leu Ser His Asn Ile
          725          730          735
Cys Asn Pro Met Thr Gly Asn Ser Leu Pro Gln Tyr Ala Glu Pro Ser
          740          745          750
Cys Pro Ser Leu Pro Ala Gly Pro Thr Gly Val Glu Glu Asp Lys Gly
          755          760          765
Leu Tyr Ser Pro Gly Asp Leu Trp Pro Thr Pro Pro Val Cys Val Thr
          770          775          780
Ser Ser Leu Asn Cys Thr Leu Glu Asn Gly Val Pro Cys Val Ile Gln
785          790          795          800
Glu Ser Ala Pro Val His Asn Ser Phe Ile Asp Trp Ser Ala Thr Cys
          805          810          815

```

Glu Gly Gln Phe Ser Ser Ala Tyr Cys Pro Leu Glu Leu Asn Asp Tyr  
                     820                    825                    830  
 Asn Ala Phe Pro Glu Glu Asn Met Asn Tyr Ala Asn Gly Phe Pro Cys  
                     835                    840                    845  
 Pro Ala Asp Val Gln Thr Asp Phe Ile Asp His Asn Ser Gln Ser Thr  
                     850                    855                    860  
 Trp Asn Thr Pro Pro Asn Met Pro Ala Ser Trp Gly Asn Ala Gln Phe  
                     865                    870                    875                    880  
 Pro Ser Ser Ser Arg Pro Tyr Leu Lys Ser Thr Pro Lys Ala Cys Leu  
                     885                    890                    895  
 Pro Met Ser Gly Leu Phe Gly Pro Ile Trp Ala Pro Gln Ser Asp Val  
                     900                    905                    910  
 Tyr Glu Asn Cys Cys Pro Ile Asn Pro Thr Thr Glu His Ser Asp Thr  
                     915                    920                    925  
 His Met Glu Asn Gln Ala Val Val Cys Lys Glu Tyr Tyr Pro Gly Phe  
                     930                    935                    940  
 Asn Pro Phe Arg Ala Tyr Met Asn Leu Asp Ile Trp Thr Thr Thr Ala  
                     945                    950                    955                    960  
 Asn Arg Asn Ala Asn Phe Pro Leu Ser Arg Asp Ser Ser Tyr Cys Gly  
                     965                    970                    975  
 Asn Val  
                     978

&lt;210&gt; 408

&lt;211&gt; 779

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 408

Asn Pro Ile Leu Trp Leu Glu Thr Gln Met Ala Ser Asn Glu Arg Asp  
   1                    5                    10                    15  
 Ala Ile Ser Trp Tyr Gln Lys Lys Ile Gly Ala Tyr Asp Gln Gln Ile  
                     20                    25                    30  
 Trp Glu Lys Ser Ile Glu Gln Thr Gln Ile Lys Gly Leu Lys Asn Lys  
                     35                    40                    45  
 Pro Lys Lys Met Gly His Ile Lys Pro Asp Leu Ile Asp Val Asp Leu  
                     50                    55                    60  
 Ile Arg Gly Ser Thr Phe Ala Lys Ala Lys Pro Glu Ile Pro Trp Thr  
                     65                    70                    75                    80  
 Ser Leu Thr Arg Lys Gly Leu Val Arg Val Val Phe Phe Pro Leu Phe  
                     85                    90                    95  
 Ser Asn Trp Trp Ile Gln Val Thr Ser Leu Arg Ile Phe Val Trp Leu  
                     100                    105                    110  
 Leu Leu Leu Tyr Phe Met Gln Val Ile Ala Ile Val Leu Tyr Leu Met  
                     115                    120                    125  
 Met Pro Ile Val Asn Ile Ser Glu Val Leu Gly Pro Leu Cys Leu Met  
                     130                    135                    140  
 Leu Leu Met Gly Thr Val His Cys Gln Ile Val Ser Thr Gln Ile Thr  
                     145                    150                    155                    160  
 Arg Pro Ser Gly Asn Asn Gly Asn Arg Arg Arg Lys Leu Arg Lys  
                     165                    170                    175  
 Thr Val Asn Gly Asp Gly Ser Arg Glu Asn Gly Asn Asn Ser Ser Asp  
                     180                    185                    190  
 Lys Val Arg Gly Ile Glu Thr Leu Glu Ser Val Pro Ile Ile Gly Gly  
                     195                    200                    205  
 Phe Trp Glu Thr Ile Phe Gly Asn Arg Ile Lys Arg Val Lys Leu Ile  
                     210                    215                    220  
 Ser Asn Lys Gly Thr Glu Thr Asp Asn Asp Pro Ser Cys Val His Pro  
                     225                    230                    235                    240  
 Ile Ile Lys Arg Arg Gln Cys Arg Pro Glu Ile Arg Met Trp Gln Thr  
                     245                    250                    255

Arg Glu Lys Ala Lys Phe Ser Asp Gly Glu Lys Cys Arg Arg Glu Ala  
 260 265 270  
 Phe Arg Arg Leu Gly Asn Gly Val Ser Asp Asp Leu Ser Ser Glu Glu  
 275 280 285  
 Asp Gly Glu Ala Arg Thr Gln Met Ile Leu Leu Arg Arg Ser Val Glu  
 290 295 300  
 Gly Ala Ser Ser Asp Asn Gly Cys Glu Val Lys Asn Arg Lys Ser Ile  
 305 310 315 320  
 Leu Ser Arg His Leu Asn Ser Gln Val Lys Lys Thr Thr Thr Arg Trp  
 325 330 335  
 Cys His Ile Val Arg Asp Ser Asp Ser Leu Ala Glu Ser Glu Phe Glu  
 340 345 350  
 Ser Ala Ala Phe Ser Gln Gly Ser Arg Ser Gly Val Ser Gly Gly Ser  
 355 360 365  
 Arg Ser Leu Asn Met Ser Arg Arg Asp Ser Glu Ser Thr Arg His Asp  
 370 375 380  
 Ser Glu Thr Glu Asp Met Leu Trp Asp Asp Leu Leu His Gly Pro Glu  
 385 390 395 400  
 Cys Arg Ser Ser Val Thr Ser Asp Ser Glu Gly Ala His Val Asn Thr  
 405 410 415  
 Leu His Ser Gly Thr Lys Arg Asp Pro Lys Glu Asp Val Phe Gln Gln  
 420 425 430  
 Asn His Leu Phe Trp Leu Gln Asn Ser Ser Pro Ser Ser Asp Arg Val  
 435 440 445  
 Ser Ala Ile Ile Trp Glu Gly Asn Glu Cys Lys Lys Met Asp Met Ser  
 450 455 460  
 Val Leu Glu Ile Ser Gly Ile Ile Met Ser Arg Val Asn Ala Tyr Gln  
 465 470 475 480  
 Gln Gly Val Gly Tyr Gln Met Leu Gly Asn Val Val Thr Ile Gly Leu  
 485 490 495  
 Ala Phe Phe Pro Phe Leu His Arg Leu Phe Arg Glu Lys Ser Leu Asp  
 500 505 510  
 Gln Leu Lys Ser Ile Ser Ala Glu Glu Ile Leu Thr Leu Phe Cys Gly  
 515 520 525  
 Ala Pro Pro Val Thr Pro Ile Ile Val Leu Ser Ile Ile Asn Phe Phe  
 530 535 540  
 Glu Arg Leu Cys Leu Thr Trp Met Phe Phe Phe Met Met Cys Val Ala  
 545 550 555 560  
 Glu Arg Thr Tyr Lys Gln Arg Phe Leu Phe Ala Lys Leu Phe Ser His  
 565 570 575  
 Ile Tyr Phe Cys Gln Gly Lys Leu Gly Lys Tyr Glu Ile Pro His Phe  
 580 585 590  
 Arg Leu Lys Lys Val Glu Asn Ile Lys Ile Trp Leu Ser Leu Arg Ser  
 595 600 605  
 Tyr Leu Lys Arg Arg Gly Pro Gln Arg Ser Val Asp Val Val Val Ser  
 610 615 620  
 Ser Val Phe Leu Leu Thr Leu Ser Ile Ala Phe Ile Cys Cys Ala Gln  
 625 630 635 640  
 Val Leu Gln Gly His Lys Thr Ser Trp Asn Asp Ala Tyr Asn Trp Gly  
 645 650 655  
 Val Phe Asp Leu Gly Glu Thr Ala Leu Leu Phe Leu Leu Arg Leu  
 660 665 670  
 Ala Ser Leu Gly Ser Glu Thr Asn Lys Lys Tyr Ser Asn Val Ser Ile  
 675 680 685  
 Leu Leu Thr Glu Gln Ile Asn Leu Tyr Leu Lys Met Glu Lys Lys Pro  
 690 695 700  
 Asn Lys Lys Glu Gln Leu Thr Leu Val Asn Asn Val Leu Lys Leu Ser  
 705 710 715 720  
 Thr Lys Leu Leu Lys Glu Leu Asp Thr Pro Phe Arg Leu Tyr Gly Leu  
 725 730 735  
 Thr Met Asn Pro Leu Ile Tyr Asn Ile Thr Arg Val Val Ile Leu Ser  
 740 745 750  
 Ala Val Ser Gly Val Ile Ser Asp Leu Leu Gly Phe Asn Ile Arg Leu

755  
Trp Lys Ile Lys Ser  
770 773

760

765

<210> 409  
<211> 1048  
<212> PRT  
<213> Homo sapiens

<400> 409  
Leu Ser Arg Ser Ser Asp Asn Asn Thr Asn Thr Leu Gly Arg Asn  
1 5 10 15  
Val Met Ser Thr Ala Thr Ser Pro Leu Met Gly Ala Gln Ser Phe Pro  
20 25 30  
Asn Leu Thr Thr Pro Gly Thr Thr Ser Thr Val Thr Met Ser Thr Ser  
35 40 45  
Ser Val Thr Ser Ser Ser Asn Val Ala Thr Ala Thr Thr Val Leu Ser  
50 55 60  
Val Gly Gln Ser Leu Ser Asn Thr Leu Thr Thr Ser Leu Thr Ser Thr  
65 70 75 80  
Ser Ser Glu Ser Asp Thr Gly Gln Glu Ala Glu Tyr Ser Leu Tyr Asp  
85 90 95  
Phe Leu Asp Ser Cys Arg Ala Ser Thr Leu Leu Ala Glu Leu Asp Asp  
100 105 110  
Asp Glu Asp Leu Pro Glu Pro Asp Glu Glu Asp Asp Glu Asn Glu Asp  
115 120 125  
Asp Asn Gln Glu Asp Gln Glu Tyr Glu Glu Val Met Ile Leu Arg Arg  
130 135 140  
Pro Ser Leu Gln Arg Arg Ala Gly Ser Arg Ser Asp Val Thr His His  
145 150 155 160  
Ala Val Thr Ser Gln Leu Pro Gln Val Pro Ala Gly Ala Gly Ser Arg  
165 170 175  
Pro Ile Gly Glu Gln Glu Glu Glu Tyr Glu Thr Lys Gly Gly Arg  
180 185 190  
Arg Arg Thr Trp Asp Asp Asp Tyr Val Leu Lys Arg Gln Phe Ser Ala  
195 200 205  
Leu Val Pro Ala Phe Asp Pro Arg Pro Gly Arg Thr Asn Val Gln Gln  
210 215 220  
Thr Thr Asp Leu Glu Ile Pro Pro Pro Gly Thr Pro His Ser Glu Leu  
225 230 235 240  
Leu Glu Glu Val Glu Cys Thr Pro Ser Pro Arg Leu Ala Leu Thr Leu  
245 250 255  
Lys Val Thr Gly Leu Gly Thr Thr Arg Glu Val Glu Leu Pro Leu Thr  
260 265 270  
Asn Phe Arg Ser Thr Ile Phe Tyr Tyr Val Gln Lys Leu Leu Gln Leu  
275 280 285  
Ser Cys Asn Gly Asn Val Lys Ser Asp Lys Leu Arg Arg Ile Trp Glu  
290 295 300  
Pro Thr Tyr Thr Ile Met Tyr Arg Glu Met Lys Asp Ser Asp Lys Glu  
305 310 315 320  
Lys Glu Asn Gly Lys Met Gly Cys Trp Ser Ile Glu His Val Glu Gln  
325 330 335  
Tyr Leu Gly Thr Asp Glu Leu Pro Lys Asn Asp Leu Ile Thr Tyr Leu  
340 345 350  
Gln Lys Asn Ala Asp Ala Ala Phe Leu Arg His Trp Lys Leu Thr Gly  
355 360 365  
Thr Asn Lys Ser Ile Arg Lys Asn Arg Asn Cys Ser Gln Leu Ile Ala  
370 375 380  
Ala Tyr Trp Asp Leu Gly Glu His Gly Thr Lys Ser Gly Leu Asn Gln  
385 390 395 400  
Gly Ala Ile Ser Thr Leu Gln Ser Ser Asp Ile Leu Asn Leu Thr Lys

```

      405      410      415
Glu Gln Pro Gln Ala Lys Ala Gly Asn Gly Gln Asn Ser Cys Gly Val
      420      425      430
Glu Asp Val Leu Gln Leu Leu Arg Ile Leu Tyr Ile Val Ala Ser Asp
      435      440      445
Pro Tyr Ser Arg Ile Ser Gln Glu Asp Gly Asp Glu Gln Pro Gln Phe
      450      455      460
Thr Phe Pro Pro Asp Glu Phe Thr Ser Lys Lys Ile Thr Thr Lys Ile
465      470      475      480
Leu Gln Gln Ile Glu Glu Pro Leu Ala Leu Ala Ser Gly Ala Leu Pro
      485      490      495
Asp Trp Cys Glu Gln Leu Thr Ser Lys Cys Pro Phe Leu Ile Pro Phe
      500      505      510
Glu Thr Arg Gln Leu Tyr Phe Thr Cys Thr Ala Phe Gly Ala Ser Arg
      515      520      525
Ala Ile Val Trp Leu Gln Asn Arg Arg Glu Ala Thr Val Glu Arg Thr
      530      535      540
Arg Thr Thr Ser Ser Val Arg Arg Asp Asp Pro Gly Glu Phe Arg Val
545      550      555      560
Gly Arg Leu Lys His Glu Arg Val Lys Val Pro Arg Gly Glu Ser Leu
      565      570      575
Met Glu Trp Ala Glu Asn Val Met Gln Ile His Ala Asp Arg Lys Ser
      580      585      590
Val Leu Glu Val Glu Phe Leu Gly Glu Glu Gly Thr Gly Leu Gly Pro
      595      600      605
Thr Leu Glu Phe Tyr Ala Leu Val Ala Ala Glu Phe Gln Arg Thr Asp
      610      615      620
Leu Gly Ala Trp Leu Cys Asp Asp Asn Phe Pro Asp Asp Glu Ser Arg
625      630      635      640
His Val Asp Leu Gly Gly Gly Leu Lys Pro Pro Gly Tyr Tyr Val Gln
      645      650      655
Arg Ser Cys Gly Leu Phe Thr Ala Pro Phe Pro Gln Asp Ser Asp Glu
      660      665      670
Leu Glu Arg Ile Thr Lys Leu Phe His Phe Leu Gly Ile Phe Leu Ala
      675      680      685
Lys Cys Ile Gln Asp Asn Arg Leu Val Asp Leu Pro Ile Ser Lys Pro
      690      695      700
Phe Phe Lys Leu Met Cys Met Gly Asp Ile Lys Ser Asn Met Ser Lys
705      710      715      720
Leu Ile Tyr Glu Ser Arg Gly Asp Arg Asp Leu His Cys Thr Glu Ser
      725      730      735
Gln Ser Glu Ala Ser Thr Glu Glu Gly His Asp Ser Leu Ser Val Gly
      740      745      750
Ser Phe Glu Glu Asp Ser Lys Ser Glu Phe Ile Leu Asp Pro Pro Lys
      755      760      765
Pro Lys Pro Pro Ala Trp Phe Asn Gly Ile Leu Thr Trp Glu Asp Phe
      770      775      780
Glu Leu Val Asn Pro His Arg Ala Arg Phe Leu Lys Glu Ile Lys Asp
785      790      795      800
Leu Ala Ile Lys Arg Arg Gln Ile Leu Ser Asn Lys Gly Leu Ser Glu
      805      810      815
Asp Glu Lys Asn Thr Lys Leu Gln Glu Leu Val Leu Lys Asn Pro Ser
      820      825      830
Gly Ser Gly Pro Pro Leu Ser Ile Glu Asp Leu Gly Leu Asn Phe Gln
      835      840      845
Phe Cys Pro Ser Ser Arg Ile Tyr Gly Phe Thr Ala Val Asp Leu Lys
      850      855      860
Pro Ser Gly Glu Asp Glu Met Ile Thr Met Asp Asn Ala Glu Glu Tyr
865      870      875      880
Val Asp Leu Met Phe Asp Phe Cys Met His Thr Gly Ile Gln Lys Gln
      885      890      895
Met Glu Ala Phe Arg Asp Gly Phe Asn Lys Val Phe Pro Met Glu Lys
      900      905      910

```

Leu Ser Ser Phe Ser His Glu Glu Val Gln Met Ile Leu Cys Gly Asn  
           915                          920                  925  
 Gln Ser Pro Ser Trp Ala Ala Glu Asp Ile Ile Asn Tyr Thr Glu Pro  
       930                          935                  940  
 Lys Leu Gly Tyr Thr Arg Asp Ser Pro Gly Phe Leu Arg Phe Val Arg  
 945                          950                  955                  960  
 Val Leu Cys Gly Met Ser Ser Asp Glu Arg Lys Ala Phe Leu Gln Phe  
                           965                          970                  975  
 Thr Thr Gly Cys Ser Thr Leu Pro Pro Gly Gly Leu Ala Asn Leu His  
                           980                          985                  990  
 Pro Arg Leu Thr Val Val Arg Lys Val Asp Ala Thr Asp Ala Ser Tyr  
                           995                         1000                 1005  
 Pro Ser Val Asn Thr Cys Val His Tyr Leu Lys Leu Pro Glu Tyr Ser  
       1010                         1015                 1020  
 Ser Glu Glu Ile Met Arg Glu Arg Leu Leu Ala Ala Thr Met Glu Lys  
 1025                         1030                         1035                 1040  
 Gly Phe His Leu Asn  
                          1045

&lt;210&gt; 410

&lt;211&gt; 629

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 410

Met Ser Pro Val Phe Pro Met Leu Thr Val Leu Thr Met Phe Tyr Tyr  
   1                          5                         10                 15  
 Ile Cys Leu Arg Arg Arg Ala Arg Thr Ala Thr Arg Gly Glu Met Met  
                          20                         25                 30  
 Asn Thr His Arg Ala Ile Glu Ser Asn Ser Gln Thr Ser Pro Leu Asn  
       35                         40                 45  
 Ala Glu Val Val Gln Tyr Ala Lys Glu Val Val Asp Phe Ser Ser His  
       50                         55                 60  
 Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met Trp Asn Leu Ala Gly  
       65                         70                 75                 80  
 Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe Thr Gln Thr Ala Val  
                          85                         90                 95  
 Phe Arg Thr Tyr Gly Thr Trp Trp Asp Gln Cys Pro Ser Ala Ser Leu  
                          100                 105                 110  
 Pro Phe Lys Arg Thr Pro Pro Asn Phe Gln Ser Gln Asp Tyr Val Glu  
                          115                 120                 125  
 Leu Thr Phe Glu Gln Gln Val Tyr Pro Thr Ala Val His Val Leu Glu  
       130                         135                 140  
 Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu Ala Cys Ser Ala Asn  
 145                         150                 155                 160  
 Pro Tyr Ser Pro Asn Pro Pro Ala Glu Val Arg Trp Glu Ile Leu Trp  
                          165                 170                 175  
 Ser Glu Arg Pro Thr Lys Val Asn Ala Ser Gln Ala Arg Gln Phe Lys  
                          180                 185                 190  
 Pro Cys Ile Lys Gln Ile Asn Phe Pro Thr Asn Leu Ile Arg Leu Glu  
       195                         200                 205  
 Val Asn Ser Ser Leu Leu Glu Tyr Tyr Thr Glu Leu Asp Ala Val Val  
       210                         215                 220  
 Leu His Gly Val Lys Asp Lys Pro Val Leu Ser Leu Lys Thr Ser Leu  
 225                         230                 235                 240  
 Ile Asp Met Asn Asp Ile Glu Asp Asp Ala Tyr Gly Arg Lys Gly Met  
                          245                 250                 255  
 Gly Cys Gly Asn Gly Thr Val Leu Asn Lys Lys Phe Ser Ser Ala Leu  
                          260                 265                 270  
 Ser Leu Gly Glu Gly Pro Asn Asn Gly Tyr Phe Asp Lys Leu Pro Tyr  
       275                         280                 285

Glu Leu Ile Gln Leu Ile Leu Asn His Leu Thr Leu Pro Asp Leu Cys  
 290 295 300  
 Arg Leu Ala Gln Thr Cys Lys Leu Leu Ser Gln His Cys Cys Asp Pro  
 305 310 315 320  
 Leu Gln Tyr Ile His Leu Asn Leu Gln Pro Tyr Trp Ala Lys Leu Asp  
 325 330 335  
 Asp Thr Ser Leu Glu Phe Leu Gln Ser Arg Cys Thr Leu Val Gln Trp  
 340 345 350  
 Leu Asn Leu Ser Trp Thr Gly Asn Arg Gly Phe Ile Ser Val Ala Gly  
 355 360 365  
 Phe Ser Arg Phe Leu Glu Gly Phe Val Gly Ser Glu Leu Val Arg Leu  
 370 375 380  
 Glu Leu Ser Cys Ser His Phe Leu Asn Glu Thr Cys Leu Glu Val Ile  
 385 390 395 400  
 Ser Glu Met Cys Pro Asn Leu Gln Ala Leu Asn Leu Ser Ser Cys Asp  
 405 410 415  
 Lys Leu Pro Pro Gln Ala Phe Asn His Ile Ala Lys Leu Cys Ser Leu  
 420 425 430  
 Lys Arg Leu Val Leu Tyr Arg Thr Lys Val Glu Gln Thr Ala Leu Leu  
 435 440 445  
 Ser Ile Leu Asn Phe Cys Ser Glu Leu Gln His Leu Ser Leu Gly Ser  
 450 455 460  
 Cys Val Met Ile Glu Asp Tyr Asp Val Ile Ala Ser Met Ile Gly Ala  
 465 470 475 480  
 Lys Cys Lys Lys Leu Arg Thr Leu Asp Leu Trp Arg Cys Lys Asn Ile  
 485 490 495  
 Thr Glu Asn Gly Ile Ala Glu Leu Ala Ser Gly Cys Pro Leu Leu Glu  
 500 505 510  
 Glu Leu Asp Leu Gly Trp Cys Pro Thr Leu Gln Ser Ser Thr Gly Cys  
 515 520 525  
 Phe Thr Arg Leu Ala His Gln Leu Pro Asn Leu Gln Lys Leu Phe Leu  
 530 535 540  
 Thr Ala Asn Arg Ser Val Cys Asp Thr Asp Ile Asp Glu Leu Ala Cys  
 545 550 555 560  
 Asn Cys Thr Arg Leu Gln Gln Leu Asp Ile Leu Gly Thr Arg Met Val  
 565 570 575  
 Ser Pro Ala Ser Leu Arg Lys Leu Leu Glu Ser Cys Lys Asp Leu Ser  
 580 585 590  
 Leu Leu Asp Val Ser Phe Cys Ser Gln Ile Asp Asn Arg Ala Val Leu  
 595 600 605  
 Glu Leu Asn Ala Ser Phe Pro Lys Val Phe Ile Lys Lys Ser Phe Thr  
 610 615 620  
 Gln  
 625

<210> 411  
 <211> 992  
 <212> PRT  
 <213> Homo sapiens

<400> 411  
 Ser Leu Gln Arg Leu Pro Gly Leu Met His Asn Leu Gln Thr Phe Leu  
 1 5 10 15  
 Leu Asp Gly Asn Phe Leu Gln Ser Leu Pro Ala Glu Leu Glu Asn Met  
 20 25 30  
 Lys Gln Leu Ser Tyr Leu Gly Leu Ser Phe Asn Glu Phe Thr Asp Ile  
 35 40 45  
 Pro Glu Val Leu Glu Lys Leu Thr Ala Val Asp Lys Leu Cys Met Ser  
 50 55 60  
 Gly Asn Cys Val Glu Thr Leu Arg Leu Gln Ala Leu Arg Lys Met Pro  
 65 70 75 80



His Ile Lys His Val Asp Leu Arg Leu Asn Val Ile Arg Lys Leu Ile  
                             85                            90                            95  
 Ala Asp Glu Val Asp Phe Leu Gln His Val Thr Gln Leu Asp Leu Arg  
                             100                            105                            110  
 Asp Asn Lys Leu Gly Asp Leu Asp Ala Met Ile Phe Asn Asn Ile Glu  
                             115                            120                            125  
 Val Leu His Cys Glu Arg Asn Gln Leu Val Thr Leu Asp Ile Cys Gly  
                             130                            135                            140  
 Tyr Phe Leu Lys Ala Leu Tyr Ala Ser Ser Asn Glu Leu Val Gln Leu  
                             145                            150                            155                            160  
 Asp Val Tyr Pro Val Pro Asn Tyr Leu Ser Tyr Met Asp Val Ser Arg  
                             165                            170                            175  
 Asn Arg Leu Glu Asn Val Pro Glu Trp Val Cys Glu Ser Arg Lys Leu  
                             180                            185                            190  
 Glu Val Leu Asp Ile Gly His Asn Gln Ile Cys Glu Leu Pro Ala Arg  
                             195                            200                            205  
 Leu Phe Cys Asn Ser Ser Leu Arg Lys Leu Leu Ala Gly His Asn Gln  
                             210                            215                            220  
 Leu Ala Arg Leu Pro Glu Arg Leu Glu Arg Thr Ser Val Glu Val Leu  
                             225                            230                            235                            240  
 Asp Val Gln His Asn Gln Leu Leu Glu Leu Pro Pro Asn Leu Leu Met  
                             245                            250                            255  
 Lys Ala Asp Ser Leu Arg Phe Leu Asn Ala Ser Ala Asn Lys Leu Glu  
                             260                            265                            270  
 Ser Leu Pro Pro Ala Thr Leu Ser Glu Glu Thr Asn Ser Ile Leu Gln  
                             275                            280                            285  
 Glu Leu Tyr Leu Thr Asn Asn Ser Leu Thr Asp Lys Cys Val Pro Leu  
                             290                            295                            300  
 Leu Thr Gly His Pro His Leu Lys Ile Leu His Met Ala Tyr Asn Arg  
                             305                            310                            315                            320  
 Leu Gln Ser Phe Pro Ala Ser Lys Met Ala Lys Leu Glu Glu Leu Glu  
                             325                            330                            335  
 Glu Ile Asp Leu Ser Gly Asn Lys Leu Lys Ala Ile Pro Thr Thr Ile  
                             340                            345                            350  
 Met Asn Cys Arg Arg Met His Thr Val Ile Ala His Ser Asn Cys Ile  
                             355                            360                            365  
 Glu Val Phe Pro Glu Val Met Gln Leu Pro Glu Ile Lys Cys Val Asp  
                             370                            375                            380  
 Leu Ser Cys Asn Glu Leu Ser Glu Val Thr Leu Pro Glu Asn Leu Pro  
                             385                            390                            395                            400  
 Pro Lys Leu Gln Glu Leu Asp Leu Thr Gly Asn Pro Arg Leu Val Leu  
                             405                            410                            415  
 Asp His Lys Thr Leu Glu Leu Leu Asn Asn Ile Arg Cys Phe Lys Ile  
                             420                            425                            430  
 Asp Gln Pro Ser Thr Gly Asp Ala Ser Gly Ala Pro Ala Val Trp Ser  
                             435                            440                            445  
 His Gly Tyr Thr Glu Ala Ser Gly Val Lys Asn Lys Leu Cys Val Ala  
                             450                            455                            460  
 Ala Leu Ser Val Asn Asn Phe Cys Asp Asn Arg Glu Ala Leu Tyr Gly  
                             465                            470                            475                            480  
 Val Phe Asp Gly Asp Arg Asn Val Glu Val Pro Tyr Leu Leu Gln Cys  
                             485                            490                            495  
 Thr Met Ser Asp Ile Leu Ala Glu Glu Leu Gln Lys Lys Thr Lys Asn  
                             500                            505                            510  
 Glu Glu Glu Tyr Met Val Asn Thr Phe Ile Val Met Gln Arg Lys Leu  
                             515                            520                            525  
 Gly Thr Ala Gly Gln Lys Leu Gly Gly Ala Ala Val Leu Cys His Ile  
                             530                            535                            540  
 Lys His Asp Pro Val Asp Pro Gly Gly Ser Phe Thr Leu Thr Ser Ala  
                             545                            550                            555                            560  
 Asn Val Gly Lys Cys Gln Thr Val Leu Cys Arg Asn Gly Lys Pro Leu  
                             565                            570                            575  
 Pro Leu Ser Arg Ser Tyr Ile Met Ser Cys Glu Glu Glu Leu Lys Arg

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      580      585      590
Ile Lys Gln His Lys Ala Ile Ile Thr Glu Asp Gly Lys Val Asn Gly
      595      600      605
Val Thr Glu Ser Thr Arg Ile Leu Gly Tyr Thr Phe Leu His Pro Ser
      610      615      620
Val Val Pro Arg Pro His Val Gln Ser Val Leu Leu Thr Pro Gln Asp
      625      630      635      640
Glu Phe Phe Ile Leu Gly Ser Lys Gly Leu Trp Asp Ser Leu Ser Val
      645      650      655
Glu Glu Ala Val Glu Ala Val Arg Asn Val Pro Asp Ala Leu Ala Ala
      660      665      670
Ala Lys Lys Leu Cys Thr Leu Ala Gln Ser Tyr Gly Cys His Asp Ser
      675      680      685
Ile Ser Ala Val Val Val Gln Leu Ser Val Thr Glu Asp Ser Phe Cys
      690      695      700
Cys Cys Glu Leu Ser Ala Gly Gly Ala Val Pro Pro Pro Ser Pro Gly
      705      710      715      720
Ile Phe Pro Pro Ser Val Asn Met Val Ile Lys Asp Arg Pro Ser Asp
      725      730      735
Gly Leu Gly Val Pro Ser Ser Ser Ser Gly Met Ala Ser Glu Ile Ser
      740      745      750
Ser Glu Leu Ser Thr Ser Glu Met Ser Ser Glu Val Gly Ser Thr Ala
      755      760      765
Ser Asp Glu Pro Pro Pro Gly Ala Leu Ser Glu Asn Ser Pro Ala Tyr
      770      775      780
Pro Ser Glu Gln Arg Cys Met Leu His Pro Ile Cys Leu Ser Asn Ser
      785      790      795      800
Phe Gln Arg Gln Leu Ser Ser Ala Thr Phe Ser Ser Ala Phe Ser Asp
      805      810      815
Asn Gly Leu Asp Ser Asp Asp Glu Glu Pro Ile Glu Gly Val Phe Thr
      820      825      830
Asn Gly Ser Arg Val Glu Val Glu Val Asp Ile His Cys Ser Arg Ala
      835      840      845
Lys Glu Lys Glu Lys Gln Gln His Leu Leu Gln Val Pro Ala Glu Ala
      850      855      860
Ser Asp Glu Gly Ile Val Ile Ser Ala Asn Glu Asp Glu Pro Gly Leu
      865      870      875      880
Pro Arg Lys Ala Asp Phe Ser Ala Val Gly Thr Ile Gly Arg Arg Arg
      885      890      895
Ala Asn Gly Ser Val Ala Pro Gln Glu Arg Ser His Asn Val Ile Glu
      900      905      910
Val Ala Thr Asp Ala Pro Leu Arg Lys Pro Gly Gly Tyr Phe Ala Ala
      915      920      925
Pro Ala Gln Pro Asp Pro Asp Asp Gln Phe Ile Ile Pro Pro Glu Leu
      930      935      940
Glu Glu Glu Val Lys Glu Ile Met Lys His His Gln Glu Gln Gln
      945      950      955      960
Gln Gln Gln Pro Pro Pro Pro Pro Gln Leu Gln Pro Gln Leu Pro Arg
      965      970      975
His Tyr Gln Leu Asp Gln Leu Pro Asp Tyr Tyr Asp Thr Pro Leu
      980      985      990      991

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&lt;210&gt; 412

&lt;211&gt; 649

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 412

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Arg Met Ala Ala Ile Leu Gly Asp Thr Ile Met Val Ala Lys Gly Leu
  1           5           10           15
Val Lys Leu Thr Gln Ala Ala Val Glu Thr His Leu Gln His Leu Gly

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      20      25      30
Ile Gly Gly Glu Leu Ile Met Ala Ala Arg Ala Leu Gln Ser Thr Ala
      35      40      45
Val Glu Gln Ile Gly Met Phe Leu Gly Lys Val Gln Gly Gln Asp Lys
      50      55      60
His Glu Glu Tyr Phe Ala Glu Asn Phe Gly Gly Pro Glu Gly Glu Phe
      65      70      75      80
His Phe Ser Val Pro His Ala Ala Gly Ala Ser Thr Asp Phe Ser Ser
      85      90      95
Ala Ser Ala Pro Asp Gln Ser Ala Pro Pro Ser Leu Gly His Ala His
      100      105      110
Ser Glu Gly Pro Ala Pro Ala Tyr Val Ala Ser Gly Pro Phe Arg Glu
      115      120      125
Ala Gly Phe Pro Gly Gln Ala Ser Ser Pro Leu Gly Arg Ala Asn Gly
      130      135      140
Arg Leu Phe Ala Asn Pro Arg Asp Ser Phe Ser Ala Met Gly Phe Gln
      145      150      155      160
Arg Arg Phe Phe His Gln Asp Gln Ser Pro Val Gly Gly Leu Thr Ala
      165      170      175
Glu Asp Ile Glu Lys Ala Arg Gln Ala Lys Ala Arg Pro Glu Asn Lys
      180      185      190
Gln His Lys Gln Thr Leu Ser Glu His Ala Arg Glu Arg Lys Val Pro
      195      200      205
Val Thr Arg Ile Gly Arg Leu Ala Asn Phe Gly Gly Leu Ala Val Gly
      210      215      220
Leu Gly Phe Gly Ala Leu Ala Glu Val Ala Lys Lys Ser Leu Arg Ser
      225      230      235      240
Glu Asp Pro Ser Gly Lys Lys Ala Val Leu Gly Ser Ser Pro Phe Leu
      245      250      255
Ser Glu Ala Asn Ala Glu Arg Ile Val Arg Thr Leu Cys Lys Val Arg
      260      265      270
Gly Ala Ala Leu Lys Leu Gly Gln Met Leu Ser Ile Gln Asp Asp Ala
      275      280      285
Phe Ile Asn Pro His Leu Ala Lys Ile Phe Glu Arg Val Arg Gln Ser
      290      295      300
Ala Asp Phe Met Pro Leu Lys Gln Met Met Lys Thr Leu Asn Asn Asp
      305      310      315      320
Leu Gly Pro Asn Trp Arg Asp Lys Leu Glu Tyr Phe Glu Glu Arg Pro
      325      330      335
Phe Ala Ala Ala Ser Ile Gly Gln Val His Leu Ala Arg Met Lys Gly
      340      345      350
Gly Arg Glu Val Ala Met Lys Ile Gln Tyr Pro Gly Val Ala Gln Ser
      355      360      365
Ile Asn Ser Asp Val Asn Asn Leu Met Ala Val Leu Asn Met Ser Asn
      370      375      380
Met Leu Pro Glu Gly Leu Phe Pro Glu His Leu Ile Asp Val Leu Arg
      385      390      395      400
Arg Glu Leu Ala Leu Glu Cys Asp Tyr Gln Arg Glu Ala Ala Cys Ala
      405      410      415
Arg Lys Phe Arg Asp Leu Leu Lys Gly His Pro Phe Phe Tyr Val Pro
      420      425      430
Glu Ile Val Asp Glu Leu Cys Ser Pro His Val Leu Thr Thr Glu Leu
      435      440      445
Val Ser Gly Phe Pro Leu Asp Gln Ala Glu Gly Leu Ser Gln Glu Ile
      450      455      460
Arg Asn Glu Ile Cys Tyr Asn Ile Leu Val Leu Cys Leu Arg Glu Leu
      465      470      475      480
Phe Glu Phe His Phe Met Gln Thr Asp Pro Asn Trp Ser Asn Phe Phe
      485      490      495
Tyr Asp Pro Gln Gln His Lys Val Ala Leu Leu Asp Phe Gly Ala Thr
      500      505      510
Arg Glu Tyr Asp Arg Ser Phe Thr Asp Leu Tyr Ile Gln Ile Ile Arg
      515      520      525

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Ala Ala Ala Asp Arg Asp Arg Glu Thr Val Arg Ala Lys Ser Ile Glu  
 530 535 540  
 Met Lys Phe Leu Thr Gly Tyr Glu Val Lys Val Met Glu Asp Ala His  
 545 550 555 560  
 Leu Asp Ala Ile Leu Ile Leu Gly Glu Ala Phe Ala Ser Asp Glu Pro  
 565 570 575  
 Phe Asp Phe Gly Thr Gln Ser Thr Thr Glu Lys Ile His Asn Leu Ile  
 580 585 590  
 Pro Val Met Leu Arg His Arg Leu Val Pro Pro Pro Glu Glu Thr Tyr  
 595 600 605  
 Ser Leu His Arg Lys Met Gly Gly Ser Phe Leu Ile Cys Ser Lys Leu  
 610 615 620  
 Lys Ala Arg Phe Pro Cys Lys Ala Met Phe Glu Glu Ala Tyr Ser Asn  
 625 630 635 640  
 Tyr Cys Lys Arg Gln Ala Gln Gln  
 645 648

<210> 413  
 <211> 970  
 <212> PRT  
 <213> Homo sapiens

<400> 413  
 Ser Gln Met His Cys Ser Gly Leu Ala Trp His Pro Asp Ile Ala Thr  
 1 5 10 15  
 Gln Leu Val Leu Cys Ser Glu Asp Asp Arg Leu Pro Val Ile Gln Leu  
 20 25 30  
 Trp Asp Leu Arg Phe Ala Ser Ser Pro Leu Lys Val Leu Glu Ser His  
 35 40 45  
 Ser Arg Gly Ile Leu Ser Val Ser Trp Ser Gln Ala Asp Ala Glu Leu  
 50 55 60  
 Leu Leu Thr Ser Ala Lys Asp Ser Gln Ile Leu Cys Arg Asn Leu Gly  
 65 70 75 80  
 Ser Ser Glu Val Val Tyr Lys Leu Pro Thr Gln Ser Ser Trp Cys Phe  
 85 90 95  
 Asp Val Gln Trp Trp Cys Pro Arg Asp Pro Ser Val Phe Ser Ala Ala Ser  
 100 105 110  
 Phe Asn Gly Trp Ile Ser Leu Tyr Ser Val Met Gly Arg Ser Trp Glu  
 115 120 125  
 Val Gln His Met Arg Gln Ala Asp Lys Ile Ser Ser Ser Phe Ser Lys  
 130 135 140  
 Gly Gln Pro Leu Pro Pro Leu Gln Val Pro Glu Gln Val Ala Gln Ala  
 145 150 155 160  
 Pro Leu Ile Pro Pro Leu Lys Lys Pro Pro Lys Trp Ile Arg Arg Pro  
 165 170 175  
 Thr Gly Val Ser Phe Ala Phe Gly Gly Lys Leu Val Thr Phe Gly Leu  
 180 185 190  
 Pro Ser Thr Pro Ala His Leu Val Pro Gln Pro Cys Pro Arg Leu Val  
 195 200 205  
 Phe Ile Ser Gln Val Thr Thr Glu Ser Glu Phe Leu Met Arg Ser Ala  
 210 215 220  
 Glu Leu Gln Glu Ala Leu Gly Ser Gly Asn Leu Leu Asn Tyr Cys Gln  
 225 230 235 240  
 Asn Lys Ser Gln Gln Ala Leu Leu Gln Ser Glu Lys Met Leu Trp Gln  
 245 250 255  
 Phe Leu Lys Val Thr Leu Glu Gln Asp Ser Arg Met Lys Phe Leu Lys  
 260 265 270  
 Leu Leu Gly Tyr Ser Lys Asp Glu Leu Gln Lys Lys Val Ala Thr Trp  
 275 280 285  
 Leu Lys Ser Asp Val Gly Leu Gly Glu Ser Pro Gln Pro Lys Gly Asn  
 290 295 300

Asp Leu Asn Ser Asp Arg Gln Gln Ala Phe Cys Ser Gln Ala Ser Lys  
 305 310 315 320  
 His Thr Thr Lys Glu Ala Ser Ala Ser Ser Ala Phe Phe Asp Glu Leu  
 325 330 335  
 Val Pro Gln Asn Met Thr Pro Trp Glu Ile Pro Ile Thr Lys Asp Ile  
 340 345 350  
 Asp Gly Leu Leu Ser Gln Ala Leu Leu Leu Gly Glu Leu Gly Pro Ala  
 355 360 365  
 Val Glu Leu Cys Leu Lys Glu Glu Arg Phe Ala Asp Ala Ile Ile Leu  
 370 375 380  
 Ala Gln Ala Gly Gly Thr Asp Leu Leu Lys Gln Thr Gln Glu Arg Tyr  
 385 390 395 400  
 Leu Ala Lys Lys Lys Thr Lys Ile Ser Ser Leu Leu Ala Cys Val Val  
 405 410 415  
 Gln Lys Asn Trp Lys Asp Val Val Cys Thr Cys Ser Leu Lys Asn Trp  
 420 425 430  
 Arg Glu Ala Leu Ala Leu Leu Leu Thr Tyr Ser Gly Thr Glu Lys Phe  
 435 440 445  
 Pro Glu Leu Cys Asp Met Leu Gly Thr Arg Met Glu Gln Glu Gly Ser  
 450 455 460  
 Arg Ala Leu Thr Ser Glu Ala Arg Leu Cys Tyr Val Cys Ser Gly Ser  
 465 470 475 480  
 Val Glu Arg Leu Val Glu Cys Trp Ala Lys Cys His Gln Ala Leu Ser  
 485 490 495  
 Pro Met Ala Leu Gln Asp Leu Met Glu Lys Val Met Val Leu Asn Arg  
 500 505 510  
 Ser Leu Glu Gln Leu Arg Gly Pro His Gly Val Ser Pro Gly Pro Ala  
 515 520 525  
 Thr Thr Tyr Arg Val Thr Gln Tyr Ala Asn Leu Leu Ala Ala Gln Gly  
 530 535 540  
 Ser Leu Ala Thr Ala Met Ser Phe Leu Pro Arg Asp Cys Ala Gln Pro  
 545 550 555 560  
 Pro Val Gln Gln Leu Arg Asp Arg Leu Phe His Ala Gln Gly Ser Ala  
 565 570 575  
 Val Leu Gly Gln Gln Ser Pro Pro Phe Pro Phe Pro Arg Ile Val Val  
 580 585 590  
 Gly Val Thr Leu His Ser Lys Glu Thr Ser Ser Tyr Arg Leu Gly Ser  
 595 600 605  
 Gln Pro Ser His Gln Val Pro Thr Pro Ser Pro Arg Pro Arg Val Phe  
 610 615 620  
 Thr Pro Gln Ser Ser Pro Ala Met Pro Leu Ala Pro Ser His Pro Ser  
 625 630 635 640  
 Pro Tyr Gln Gly Pro Arg Thr Gln Asn Ile Ser Asp Tyr Arg Ala Pro  
 645 650 655  
 Gly Pro Gln Ala Ile Gln Pro Leu Pro Leu Ser Pro Gly Val Arg Pro  
 660 665 670  
 Ala Ser Ser Gln Pro Gln Leu Leu Gly Gly Gln Arg Val Gln Val Pro  
 675 680 685  
 Asn Pro Val Gly Phe Pro Gly Thr Trp Pro Leu Pro Gly Ser Pro Leu  
 690 695 700  
 Pro Met Ala Cys Pro Gly Ile Met Arg Pro Gly Ser Thr Ser Leu Pro  
 705 710 715 720  
 Glu Thr Pro Arg Leu Phe Pro Leu Leu Pro Leu Arg Pro Leu Gly Pro  
 725 730 735  
 Gly Arg Met Val Ser His Thr Pro Ala Pro Pro Ala Ser Phe Pro Val  
 740 745 750  
 Pro Tyr Leu Pro Gly Asp Pro Gly Ala Pro Cys Ser Ser Val Leu Pro  
 755 760 765  
 Thr Thr Gly Ile Leu Thr Pro His Pro Gly Pro Gln Asp Ser Trp Lys  
 770 775 780  
 Glu Ala Pro Ala Pro Arg Gly Asn Leu Gln Arg Asn Lys Leu Pro Glu  
 785 790 795 800  
 Thr Phe Met Pro Pro Ala Pro Ile Thr Ala Pro Val Met Ser Leu Thr

```

      805      810      815
Pro Glu Leu Gln Gly Ile Leu Pro Ser Gln Pro Pro Val Ser Ser Val
      820      825      830
Ser His Ala Pro Pro Gly Val Pro Gly Glu Leu Ser Leu Gln Gln Leu
      835      840      845
Gln His Leu Pro Pro Glu Lys Met Glu Arg Lys Glu Leu Pro Pro Glu
      850      855      860
His Gln Ser Leu Lys Ser Ser Phe Glu Ala Leu Leu Gln Arg Cys Ser
      865      870      875      880
Leu Ser Ala Thr Asp Leu Lys Thr Lys Arg Lys Leu Glu Glu Ala Ala
      885      890      895
Gln Arg Leu Glu Tyr Leu Tyr Glu Lys Leu Cys Glu Gly Thr Leu Ser
      900      905      910
Pro His Val Val Ala Gly Leu His Glu Val Ala Arg Cys Val Asp Ala
      915      920      925
Gly Ser Phe Glu Gln Gly Leu Ala Val His Ala Gln Val Ala Gly Cys
      930      935      940
Ser Ser Phe Ser Glu Val Ser Ser Phe Met Pro Ile Leu Lys Ala Val
      945      950      955      960
Leu Ile Ile Ala His Lys Leu Leu Val
      965      969

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<210> 414  
 <211> 367  
 <212> PRT  
 <213> Homo sapiens

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      <400> 414
Ile Ser Leu Phe Met Gly Glu Lys Arg Tyr Val Lys Lys Ile Lys Ile
  1      5      10      15
Met Ile Cys His Leu Gln Leu Pro Phe Phe Phe Leu Leu Asn Ser Ile
      20      25      30
Ser His Leu His Val Pro Phe Ser Phe Val Phe Pro Gln Asn Ser Arg
      35      40      45
Thr Arg Asp Leu Ala Leu Ala Asn Phe Leu Leu Leu Cys Thr His Thr
      50      55      60
His Thr Cys Arg Leu Ala Pro Pro Trp Ser Thr His Met Thr Ala Gly
      65      70      75      80
Ala Met Ala Gly Ile Leu Glu His Ser Val Met Tyr Pro Val Asp Ser
      85      90      95
Val Lys Thr Arg Met Gln Ser Leu Ser Pro Asp Pro Lys Ala Gln Tyr
      100      105      110
Thr Ser Ile Tyr Gly Ala Leu Lys Lys Ile Met Arg Thr Glu Gly Phe
      115      120      125
Trp Arg Pro Leu Arg Gly Val Asn Val Met Ile Met Gly Ala Gly Pro
      130      135      140
Ala His Ala Met Tyr Phe Ala Cys Tyr Glu Asn Met Lys Arg Thr Leu
      145      150      155      160
Asn Asp Val Phe His His Gln Gly Asn Ser His Leu Ala Asn Gly Ile
      165      170      175
Ala Gly Ser Met Ala Thr Leu Leu His Asp Ala Val Met Asn Pro Ala
      180      185      190
Glu Val Val Lys Gln Arg Leu Gln Met Tyr Asn Ser Gln His Arg Ser
      195      200      205
Ala Ile Ser Cys Ile Arg Thr Val Trp Arg Thr Glu Gly Leu Gly Ala
      210      215      220
Phe Tyr Arg Thr Tyr Asn Pro Gln Leu Thr Met Asn Ile Pro Phe Gln
      225      230      235      240
Ser Ile His Phe Ile Thr Tyr Glu Phe Leu Gln Glu Gln Val Asn Pro
      245      250      255
His Arg Thr Tyr Asn Pro Gln Ser His Ile Ile Ser Gly Gly Leu Ala

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260 265 270  
 Gly Ala Leu Ala Ala Ala Thr Thr Pro Leu Asp Val Cys Lys Thr  
 275 280 285  
 Leu Leu Asn Thr Gln Glu Asn Val Ala Leu Ser Leu Ala Asn Ile Ser  
 290 295 300  
 Gly Arg Leu Ser Gly Met Ala Asn Ala Phe Arg Thr Val Tyr Gln Leu  
 305 310 315 320  
 Asn Gly Leu Ala Gly Tyr Phe Lys Gly Ile Gln Ala Arg Val Ile Tyr  
 325 330 335  
 Gln Met Pro Ser Thr Ala Ile Ser Trp Ser Val Tyr Glu Phe Phe Lys  
 340 345 350  
 Tyr Phe Leu Thr Lys Arg Gln Leu Glu Asn Arg Ala Pro Tyr  
 355 360 365 366

<210> 415  
 <211> 947  
 <212> PRT  
 <213> Homo sapiens

<400> 415  
 Ser Lys Lys Met Val Phe Leu Pro Leu Lys Trp Ser Leu Ala Thr Met  
 1 5 10 15  
 Ser Phe Leu Leu Ser Ser Leu Leu Ala Leu Leu Thr Val Ser Thr Pro  
 20 25 30  
 Ser Trp Cys Gln Ser Thr Glu Ala Ser Pro Lys Arg Ser Asp Gly Thr  
 35 40 45  
 Pro Phe Pro Trp Asn Lys Ile Arg Leu Pro Glu Tyr Val Ile Pro Val  
 50 55 60  
 His Tyr Asp Leu Leu Ile His Ala Asn Leu Thr Thr Leu Thr Phe Trp  
 65 70 75 80  
 Gly Thr Thr Lys Val Glu Ile Thr Ala Ser Gln Pro Thr Ser Thr Ile  
 85 90 95  
 Ile Leu His Ser His His Leu Gln Ile Ser Arg Ala Thr Leu Arg Lys  
 100 105 110  
 Gly Ala Gly Glu Arg Leu Ser Glu Glu Pro Leu Gln Val Leu Glu His  
 115 120 125  
 Pro Pro Gln Glu Gln Ile Ala Leu Leu Ala Pro Glu Pro Leu Phe Val  
 130 135 140  
 Gly Leu Pro Tyr Thr Val Val Ile His Tyr Ala Gly Asn Leu Ser Glu  
 145 150 155 160  
 Thr Phe His Gly Phe Tyr Lys Ser Thr Tyr Arg Thr Lys Glu Gly Glu  
 165 170 175  
 Leu Arg Ile Leu Ala Ser Thr Gln Phe Glu Pro Thr Ala Ala Arg Met  
 180 185 190  
 Ala Phe Pro Cys Phe Asp Glu Pro Ala Phe Lys Ala Ser Phe Ser Ile  
 195 200 205  
 Lys Ile Arg Arg Glu Pro Arg His Leu Ala Ile Ser Asn Met Pro Leu  
 210 215 220  
 Val Lys Ser Val Thr Val Ala Glu Gly Leu Ile Glu Asp His Phe Asp  
 225 230 235 240  
 Val Pro Val Lys Met Ser Thr Tyr Leu Val Ala Phe Ile Ile Ser Asp  
 245 250 255  
 Phe Glu Ser Val Ser Lys Ile Thr Lys Ser Gly Val Lys Val Ser Val  
 260 265 270  
 Tyr Ala Val Pro Asp Lys Ile Asn Gln Ala Asp Tyr Ala Leu Asp Ala  
 275 280 285  
 Ala Val Thr Leu Leu Glu Phe Tyr Glu Asp Tyr Phe Ser Ile Pro Tyr  
 290 295 300  
 Pro Leu Pro Lys Gln Asp Leu Ala Ala Ile Pro Asp Phe Gln Ser Gly  
 305 310 315 320  
 Ala Met Glu Asn Trp Gly Leu Thr Thr Tyr Arg Glu Ser Ala Leu Leu

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      325      330      335
Phe Asp Ala Glu Lys Ser Ser Ala Ser Ser Lys Leu Gly Ile Thr Val
      340      345      350
Thr Val Ala His Glu Leu Ala His Gln Trp Phe Gly Asn Leu Val Thr
      355      360      365
Met Glu Trp Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala Lys Phe
      370      375      380
Met Glu Phe Val Ser Val Ser Val Thr His Pro Glu Leu Lys Val Gly
385      390      395      400
Asp Tyr Phe Phe Gly Lys Cys Phe Asp Ala Met Glu Val Asp Ala Leu
      405      410      415
Asn Ser Ser His Pro Val Ser Thr Pro Val Glu Asn Pro Ala Gln Ile
      420      425      430
Arg Glu Met Phe Asp Asp Val Ser Tyr Asp Lys Gly Ala Cys Ile Leu
      435      440      445
Asn Met Leu Arg Glu Tyr Leu Ser Ala Asp Ala Phe Lys Ser Gly Ile
450      455      460
Val Gln Tyr Leu Gln Lys His Ser Tyr Lys Asn Thr Lys Asn Glu Asp
465      470      475      480
Leu Trp Asp Ser Met Ala Ser Ile Cys Pro Thr Asp Gly Val Lys Gly
      485      490      495
Met Asp Gly Phe Cys Ser Arg Ser Gln His Ser Ser Ser Ser Ser His
      500      505      510
Trp His Gln Glu Gly Val Asp Val Lys Thr Met Met Asn Thr Trp Thr
      515      520      525
Leu Gln Arg Gly Phe Pro Leu Ile Thr Ile Thr Val Arg Gly Arg Asn
530      535      540
Val His Met Lys Gln Glu His Tyr Met Lys Gly Ser Asp Gly Ala Pro
545      550      555      560
Asp Thr Gly Tyr Leu Trp His Val Pro Leu Thr Phe Ile Thr Ser Lys
      565      570      575
Ser Asp Met Val His Arg Phe Leu Leu Lys Thr Lys Thr Asp Val Leu
      580      585      590
Ile Leu Pro Glu Glu Val Glu Trp Ile Lys Phe Asn Val Gly Met Asn
595      600      605
Gly Tyr Tyr Ile Val His Tyr Glu Asp Asp Gly Trp Asp Ser Leu Thr
610      615      620
Gly Leu Leu Lys Gly Thr His Thr Ala Val Ser Ser Asn Asp Arg Ala
625      630      635      640
Ser Leu Ile Asn Asn Ala Phe Gln Leu Val Ser Ile Gly Lys Leu Ser
      645      650      655
Ile Glu Lys Ala Leu Asp Leu Ser Leu Tyr Leu Lys His Glu Thr Glu
660      665      670
Ile Met Pro Val Phe Gln Gly Leu Asn Glu Leu Ile Pro Met Tyr Lys
675      680      685
Leu Met Glu Lys Arg Asp Met Asn Glu Val Glu Thr Gln Phe Lys Ala
690      695      700
Phe Leu Ile Arg Leu Leu Arg Asp Leu Ile Asp Lys Gln Thr Trp Thr
705      710      715      720
Asp Glu Gly Ser Val Ser Glu Gln Met Leu Arg Ser Glu Leu Leu Leu
      725      730      735
Leu Ala Cys Val His Asn Tyr Gln Pro Cys Val Gln Arg Ala Glu Gly
740      745      750
Tyr Phe Arg Lys Trp Lys Glu Ser Asn Gly Asn Leu Ser Leu Pro Val
755      760      765
Asp Val Thr Leu Ala Val Phe Ala Val Gly Ala Gln Ser Thr Glu Gly
770      775      780
Trp Asp Phe Leu Tyr Ser Lys Tyr Gln Phe Ser Leu Ser Ser Thr Glu
785      790      795      800
Lys Ser Gln Ile Glu Phe Ala Leu Cys Arg Thr Gln Asn Lys Glu Lys
      805      810      815
Leu Gln Trp Leu Leu Asp Glu Ser Phe Lys Gly Asp Lys Ile Lys Thr
820      825      830

```



```

Gln Glu Phe Pro Gln Ile Leu Thr Leu Ile Gly Arg Asn Pro Val Gly
      835                840                845
Tyr Pro Leu Ala Trp Gln Phe Leu Arg Lys Asn Trp Asn Lys Leu Val
      850                855                860
Gln Lys Phe Glu Leu Gly Ser Ser Ser Ile Ala His Met Val Met Gly
865      870      875      880
Thr Thr Asn Gln Phe Ser Thr Arg Thr Arg Leu Glu Glu Val Lys Gly
      885      890      895
Phe Phe Ser Ser Leu Lys Glu Asn Gly Ser Gln Leu Arg Cys Val Gln
      900      905      910
Gln Thr Ile Glu Thr Ile Glu Glu Asn Ile Gly Trp Met Asp Lys Asn
      915      920      925
Phe Asp Lys Ile Arg Val Trp Leu Gln Ser Glu Lys Leu Glu Arg Met
      930      935      940      944

```

```

<210> 416
<211> 54
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(54)
<223> Xaa = any amino acid or nothing

```

```

<400> 416
Phe Phe Val Phe Leu Val Glu Thr Gly Phe His Arg Val Ser Gln Asp
 1          5          10          15
Gly Leu Asp Leu Leu Thr Ser Xaa Ser Thr Cys Leu Gly Leu Pro Lys
      20      25      30
Cys Trp Asp Tyr Arg Cys Glu Pro Pro Arg Pro Ala Asn Ser Thr Asn
      35      40      45
Ser Xaa Glu Leu Ala Gln
      50      54

```

```

<210> 417
<211> 116
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(116)
<223> Xaa = any amino acid or nothing

```

```

<400> 417
Asp Glu Lys Pro Leu Pro Arg Ala Leu Gln Cys Pro Pro Leu His Ser
 1          5          10          15
Ala Pro Ser Thr Pro Leu Lys Phe Cys Pro Xaa Ala Thr Gly Arg Arg
      20      25      30
Pro Phe Ala Pro Ser Pro Thr His Pro Ser Leu Arg Pro Pro Pro Ser
      35      40      45
Leu Pro Thr Cys Phe Leu Pro Pro Val Pro Val Phe His Glu Ala Ala
      50      55      60
Val Ser Pro Cys Pro Cys Leu Ala Thr Leu Arg Trp Ala Pro Pro Pro
      65      70      75      80
Pro Arg Leu Ser Leu Ala Gly Val Arg Gln Ser Pro Ala Glu Gly Gly
      85      90      95
Arg Val Leu Gly Asp Pro Glu Leu Pro Pro Arg Ile Pro Pro Gln Gly

```

100 105 110  
 Leu Tyr Ser Arg  
 115 116

<210> 418  
 <211> 296  
 <212> PRT  
 <213> Homo sapiens

<400> 418  
 Cys Leu Ala Ser Arg Leu Pro Cys Ala Leu Thr Met Pro Ala Ala Thr  
 1 5 10 15  
 Val Asp His Ser Gln Arg Ile Cys Glu Val Trp Ala Cys Asn Leu Asp  
 20 25 30  
 Glu Glu Met Lys Lys Ile Arg Gln Val Ile Arg Lys Tyr Asn Tyr Val  
 35 40 45  
 Ala Met Asp Thr Glu Phe Pro Gly Val Val Ala Arg Pro Ile Gly Glu  
 50 55 60  
 Phe Arg Ser Asn Ala Asp Tyr Gln Tyr Gln Leu Leu Arg Cys Asn Val  
 65 70 75 80  
 Asp Leu Leu Lys Ile Ile Gln Leu Gly Leu Thr Phe Met Asn Glu Gln  
 85 90 95  
 Gly Glu Tyr Pro Pro Gly Thr Ser Thr Trp Gln Phe Asn Phe Lys Phe  
 100 105 110  
 Asn Leu Thr Glu Asp Met Tyr Ala Gln Asp Ser Ile Glu Leu Leu Thr  
 115 120 125  
 Thr Ser Gly Ile Gln Phe Lys Lys His Glu Glu Glu Gly Ile Glu Thr  
 130 135 140  
 Gln Tyr Phe Ala Glu Leu Leu Met Thr Ser Gly Val Val Leu Cys Glu  
 145 150 155 160  
 Gly Val Lys Trp Leu Ser Phe His Ser Gly Tyr Asp Phe Gly Tyr Leu  
 165 170 175  
 Ile Lys Ile Leu Thr Asn Ser Asn Leu Pro Glu Glu Glu Leu Asp Phe  
 180 185 190  
 Phe Glu Ile Leu Arg Leu Phe Phe Pro Val Ile Tyr Asp Val Lys Tyr  
 195 200 205  
 Leu Met Lys Ser Cys Lys Asn Leu Lys Gly Gly Leu Gln Glu Val Ala  
 210 215 220  
 Glu Gln Leu Glu Leu Glu Arg Ile Gly Pro Gln His Gln Ala Gly Ser  
 225 230 235 240  
 Asp Ser Leu Leu Thr Gly Met Ala Phe Phe Lys Met Arg Glu Met Phe  
 245 250 255  
 Phe Glu Asp His Ile Asp Asp Ala Lys Tyr Cys Gly His Leu Tyr Gly  
 260 265 270  
 Leu Gly Ser Gly Ser Ser Tyr Val Gln Asn Gly Thr Gly Asn Ala Tyr  
 275 280 285  
 Glu Glu Glu Ala Asn Lys Gln Ser  
 290 295 296

<210> 419  
 <211> 144  
 <212> PRT  
 <213> Homo sapiens

<400> 419  
 Arg Arg Leu Arg Glu Arg Asp Arg Val Ser Gly Glu Gly Gly Arg Pro  
 1 5 10 15  
 Arg Ala Gly Ile Ser Glu Ala Leu Arg Cys Ile Met Lys Phe Gln Tyr  
 20 25 30

Lys Glu Asp His Pro Phe Glu Tyr Arg Lys Lys Glu Gly Glu Lys Ile  
           35                                  40                                  45  
 Arg Lys Lys Tyr Pro Asp Arg Val Pro Val Ile Val Glu Lys Ala Pro  
           50                                  55                                  60  
 Lys Ala Arg Val Pro Asp Leu Asp Lys Arg Lys Tyr Leu Val Pro Ser  
           65                                  70                                  75                                  80  
 Asp Leu Thr Val Gly Gln Phe Tyr Phe Leu Ile Arg Lys Arg Ile His  
                                   85                                  90                                  95  
 Leu Arg Pro Glu Asp Ala Leu Phe Phe Phe Val Asn Asn Thr Ile Pro  
                                   100                                  105                                  110  
 Pro Thr Ser Ala Thr Met Gly Gln Leu Tyr Glu Asp Asn His Glu Glu  
                                   115                                  120                                  125  
 Asp Tyr Phe Leu Tyr Val Ala Tyr Ser Asp Glu Ser Val Tyr Gly Lys  
           130                                  135                                  140                                  144

&lt;210&gt; 420

&lt;211&gt; 546

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

Phe Arg Pro Thr Pro Val Pro Ser Pro Val Ser Met Val Trp Ile Pro  
   1                                  5                                  10                                  15  
 Cys Ala Val Ala Ser Phe Phe Gly Asp Ala Ser Ala Ala Ala Trp Gly  
           20                                  25                                  30  
 Gly Glu Leu Ser Gly Ser Tyr Thr Ala Thr Ala Arg Met Asp Arg Met  
           35                                  40                                  45  
 Thr Glu Asp Ala Leu Arg Leu Asn Leu Leu Lys Arg Ser Leu Asp Pro  
           50                                  55                                  60  
 Ala Asp Glu Arg Asp Asp Val Leu Ala Lys Arg Leu Lys Met Glu Gly  
           65                                  70                                  75                                  80  
 His Glu Ala Met Glu Arg Leu Lys Met Leu Ala Leu Leu Lys Arg Lys  
                                   85                                  90                                  95  
 Asp Leu Ala Asn Leu Glu Val Pro His Glu Leu Pro Thr Lys Gln Asp  
                                   100                                  105                                  110  
 Gly Ser Gly Val Lys Gly Tyr Glu Lys Leu Asn Gly Asn Leu Arg  
           115                                  120                                  125  
 Pro His Gly Asp Asn Arg Thr Ala Gly Arg Pro Gly Lys Glu Asn Ile  
           130                                  135                                  140  
 Asn Asp Glu Pro Val Asp Met Ser Ala Arg Arg Ser Glu Pro Glu Arg  
           145                                  150                                  155                                  160  
 Gly Arg Leu Thr Pro Ser Pro Asp Ile Ile Val Leu Ser Asp Asn Glu  
                                   165                                  170                                  175  
 Ala Ser Ser Pro Arg Ser Ser Ser Arg Met Glu Glu Arg Leu Lys Ala  
                                   180                                  185                                  190  
 Ala Asn Leu Glu Met Phe Lys Gly Lys Gly Ile Glu Glu Arg Gln Gln  
           195                                  200                                  205  
 Leu Ile Lys Gln Leu Arg Asp Glu Leu Arg Leu Glu Glu Ala Arg Leu  
           210                                  215                                  220  
 Val Leu Leu Lys Lys Leu Arg Gln Ser Gln Leu Gln Lys Glu Asn Val  
           225                                  230                                  235                                  240  
 Val Gln Lys Thr Pro Val Val Gln Asn Ala Ala Ser Ile Val Gln Pro  
                                   245                                  250                                  255  
 Ser Pro Ala His Val Gly Gln Gln Gly Leu Ser Lys Leu Pro Ser Arg  
                                   260                                  265                                  270  
 Pro Gly Ala Gln Gly Val Glu Pro Gln Asn Leu Arg Thr Leu Gln Gly  
           275                                  280                                  285  
 His Ser Val Ile Arg Ser Ala Thr Asn Thr Thr Leu Pro His Met Leu  
           290                                  295                                  300

Met Ser Gln Arg Val Ile Ala Pro Asn Pro Ala Gln Leu Gln Gly Gln  
 305 310 315 320  
 Arg Gly Pro Pro Lys Pro Gly Leu Val Arg Thr Thr Thr Pro Asn Met  
 325 330 335  
 Asn Pro Ala Ile Asn Tyr Gln Pro Gln Ser Ser Ser Ser Val Pro Cys  
 340 345 350  
 Gln Arg Thr Thr Ser Ser Ala Ile Tyr Met Asn Leu Ala Ser His Ile  
 355 360 365  
 Gln Pro Gly Thr Val Asn Arg Val Ser Ser Pro Leu Pro Ser Pro Ser  
 370 375 380  
 Ala Met Thr Asp Ala Ala Asn Ser Gln Ala Ala Ala Lys Leu Ala Leu  
 385 390 395 400  
 Arg Lys Gln Leu Glu Lys Thr Leu Leu Glu Ile Pro Pro Pro Lys Pro  
 405 410 415  
 Pro Ala Pro Leu Leu His Phe Leu Pro Ser Ala Ala Asn Ser Glu Phe  
 420 425 430  
 Ile Tyr Met Val Gly Leu Glu Glu Val Val Gln Ser Val Ile Asp Ser  
 435 440 445  
 Gln Gly Lys Ser Cys Ala Ser Leu Leu Arg Val Glu Pro Phe Val Cys  
 450 455 460  
 Ala Gln Cys Arg Thr Asp Phe Thr Pro His Trp Lys Gln Glu Lys Asn  
 465 470 475 480  
 Gly Lys Ile Leu Cys Glu Gln Cys Met Thr Ser Asn Gln Lys Lys Ala  
 485 490 495  
 Leu Lys Ala Glu His Thr Asn Arg Leu Lys Asn Ala Phe Val Lys Ala  
 500 505 510  
 Leu Gln Gln Glu Gln Val Arg Ile Leu Thr Ala His Trp Pro Pro Val  
 515 520 525  
 Pro Val Cys Phe Phe Gln Arg Val Ala Pro Ser Ser Leu Gln Glu Trp  
 530 535 540  
 Phe Met  
 545 546

<210> 421  
 <211> 135  
 <212> PRT  
 <213> Homo sapiens

<400> 421  
 Arg Cys Arg Ser Tyr Glu Asp Cys Cys Gly Ser Arg Cys Cys Val Arg  
 1 5 10 15  
 Ala Leu Ser Ile Gln Arg Leu Trp Tyr Phe Trp Phe Leu Leu Met Met  
 20 25 30  
 Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe Ile Arg Arg Arg Met  
 35 40 45  
 Tyr Pro Pro Pro Leu Ile Glu Glu Pro Ala Phe Asn Val Ser Tyr Thr  
 50 55 60  
 Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln Gln Pro Gly Pro Pro  
 65 70 75 80  
 Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn Pro Val Gly Asn Ser  
 85 90 95  
 Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser Pro Gln Gly Ser Val  
 100 105 110  
 Ala Cys Pro Pro Pro Pro Ala Tyr Cys Asn Thr Pro Pro Pro Pro Tyr  
 115 120 125  
 Glu Gln Val Val Lys Ala Lys  
 130 135

<210> 422  
 <211> 179

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

```

Ile Thr Met Gly Asn Ile Phe Glu Lys Leu Phe Lys Ser Leu Leu Gly
 1          5          10          15
Lys Lys Lys Met Arg Ile Leu Ile Leu Ser Leu Asp Thr Ala Gly Lys
          20          25          30
Thr Thr Ile Leu Tyr Lys Leu Lys Leu Gly Glu Thr Val Pro Ala Val
          35          40          45
Pro Thr Val Gly Phe Cys Val Glu Thr Val Glu Tyr Lys Asn Asn Thr
 50          55          60
Phe Ala Val Trp Asp Val Gly Ser His Phe Lys Ile Arg Pro Leu Trp
 65          70          75          80
Gln His Phe Phe Gln Asn Thr Lys Gly Ala Arg Ser Pro Gly Ser Thr
          85          90          95
His Gln Gly Ser Leu Ala Ser Gly Val Leu Pro Ile Lys Cys Ser His
          100          105          110
Val Glu Phe Gly Met Trp Lys Gly Gly Arg Ser His Pro Phe Leu Pro
          115          120          125
His Ser Ser Arg Cys Ala Gly Ser Gly Gly Gln Leu Asp Ser Ile Leu
          130          135          140
Pro His Gln Ser Pro Ala Trp Gly Pro Trp Gly Cys Lys Asp Leu Ser
          145          150          155          160
Ser Gly Phe Pro Ser Phe Leu Thr Ser Ser Ile Leu Trp Lys Ser Ala
          165          170          175
Val Val Lys
          179

```

&lt;210&gt; 423

&lt;211&gt; 1343

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 423

```

Arg His Pro Gly Cys Gly Ala Gly Arg Pro Gly Ala Pro Pro Pro Arg
 1          5          10          15
His Gly Ser Arg Gly Gly Arg Gly Asp Arg Ala Arg Ala Gly Gly Gly
          20          25          30
Gly Pro Ser Arg Gly Ser Gly Gly Gly Gly Arg Gly Gly Leu Arg Ala
          35          40          45
Asp Gly Arg Ala Pro Gly Leu Arg Gly Leu Gly Ala Ala Pro His Cys
 50          55          60
Pro Ala Gly Leu Gly Pro Gly Ala Met Ser Gly Gly Gly Gly Gly Gly
 65          70          75          80
Gly Ser Ala Pro Ser Arg Phe Ala Asp Tyr Phe Val Ile Cys Gly Leu
          85          90          95
Asp Thr Glu Thr Gly Leu Glu Pro Asp Glu Leu Ser Ala Leu Cys Gln
          100          105          110
Tyr Ile Gln Ala Ser Lys Ala Arg Asp Gly Ala Ser Pro Phe Ile Ser
          115          120          125
Ser Thr Thr Glu Gly Glu Asn Phe Glu Gln Thr Pro Leu Arg Arg Thr
          130          135          140
Phe Lys Ser Lys Val Leu Ala Arg Tyr Pro Glu Asn Val Glu Trp Asn
          145          150          155          160
Pro Phe Asp Gln Asp Ala Val Gly Met Leu Cys Met Pro Lys Gly Leu
          165          170          175
Ala Phe Lys Thr Gln Ala Asp Pro Arg Glu Pro Gln Phe His Ala Phe
          180          185          190
Ile Ile Thr Arg Glu Asp Gly Ser Arg Thr Phe Gly Phe Ala Leu Thr

```

313

Asp Glu Ala Glu Lys Ala Ile Glu Leu Arg Leu Ala Lys Ile Asp His  
 705 710 715 720  
 Thr Ala Ile His Pro His Leu Leu Asp Met Lys Ile Gly Gln Gly Lys  
 725 730 735  
 Tyr Glu Pro Gly Phe Phe Pro Lys Leu Gln Ser Asp Val Leu Ser Thr  
 740 745 750  
 Gly Pro Ala Ser Asn Lys Trp Thr Lys Arg Asn Ala Pro Ala Gln Trp  
 755 760 765  
 Arg Arg Lys Asp Arg Gln Lys Gln His Thr Glu His Leu Arg Leu Asp  
 770 775 780  
 Asn Asp Gln Arg Glu Lys Tyr Ile Gln Glu Ala Arg Thr Met Gly Ser  
 785 790 795 800  
 Thr Ile Arg Gln Pro Lys Leu Ser Asn Leu Ser Pro Ser Val Ile Ala  
 805 810 815  
 Gln Thr Asn Trp Lys Phe Val Glu Gly Leu Leu Lys Glu Cys Arg Asn  
 820 825 830  
 Lys Thr Lys Arg Met Leu Val Glu Lys Met Gly Arg Glu Ala Val Glu  
 835 840 845  
 Leu Gly His Gly Glu Val Asn Ile Thr Gly Val Glu Glu Asn Thr Leu  
 850 855 860  
 Ile Ala Ser Leu Cys Asp Leu Leu Glu Arg Ile Trp Ser His Gly Leu  
 865 870 875 880  
 Gln Val Lys Gln Gly Lys Ser Ala Leu Trp Ser His Leu Leu His Tyr  
 885 890 895  
 Gln Asp Asn Arg Gln Arg Lys Leu Thr Ser Gly Ser Leu Ser Thr Ser  
 900 905 910  
 Gly Ile Leu Leu Asp Ser Glu Arg Arg Lys Ser Asp Ala Ser Ser Leu  
 915 920 925  
 Met Pro Pro Leu Arg Ile Ser Leu Ile Gln Asp Met Arg His Ile Gln  
 930 935 940  
 Asn Ile Gly Glu Ile Lys Thr Asp Val Gly Lys Ala Arg Ala Trp Val  
 945 950 955 960  
 Arg Leu Ser Met Glu Lys Lys Leu Leu Ser Arg His Leu Lys Gln Leu  
 965 970 975  
 Leu Ser Asp His Glu Leu Thr Lys Lys Leu Tyr Lys Arg Tyr Ala Phe  
 980 985 990  
 Leu Arg Cys Asp Asp Glu Lys Glu Gln Phe Leu Tyr His Leu Leu Ser  
 995 1000 1005  
 Phe Asn Ala Val Asp Tyr Phe Cys Phe Thr Asn Val Phe Thr Thr Ile  
 1010 1015 1020  
 Leu Ile Pro Tyr His Ile Leu Ile Val Pro Ser Lys Lys Leu Gly Gly  
 1025 1030 1035 1040  
 Ser Met Phe Thr Ala Asn Pro Trp Ile Cys Ile Ser Gly Glu Leu Gly  
 1045 1050 1055  
 Glu Thr Gln Ile Met Gln Ile Pro Arg Asn Val Leu Glu Met Thr Phe  
 1060 1065 1070  
 Glu Cys Gln Asn Leu Gly Lys Leu Thr Thr Val Gln Ile Gly His Asp  
 1075 1080 1085  
 Asn Ser Gly Leu Tyr Ala Lys Trp Leu Val Glu Tyr Val Met Val Arg  
 1090 1095 1100  
 Asn Glu Ile Thr Gly His Thr Tyr Lys Phe Pro Cys Gly Arg Trp Leu  
 1105 1110 1115 1120  
 Gly Lys Gly Met Asp Asp Gly Ser Leu Glu Arg Ile Leu Val Gly Glu  
 1125 1130 1135  
 Leu Leu Thr Ser Gln Pro Glu Val Asp Glu Arg Pro Cys Arg Thr Pro  
 1140 1145 1150  
 Pro Leu Gln Gln Ser Pro Ser Val Ile Arg Arg Leu Val Thr Ile Ser  
 1155 1160 1165  
 Pro Asn Asn Lys Pro Lys Leu Asn Thr Gly Gln Ile Gln Glu Ser Ile  
 1170 1175 1180  
 Gly Glu Ala Val Asn Gly Ile Val Lys His Phe His Lys Pro Glu Lys  
 1185 1190 1195 1200  
 Glu Arg Gly Ser Leu Thr Leu Leu Leu Cys Gly Glu Cys Gly Leu Val

1205 1210 1215  
 Ser Ala Leu Glu Gln Ala Phe Gln His Gly Phe Lys Ser Pro Arg Leu  
 1220 1225 1230  
 Phe Lys Asn Val Phe Ile Trp Asp Phe Leu Glu Lys Ala Gln Thr Tyr  
 1235 1240 1245  
 Tyr Glu Thr Leu Glu Lys Asn Glu Val Val Pro Glu Glu Asn Trp His  
 1250 1255 1260  
 Thr Arg Ala Arg Asn Phe Cys Arg Phe Val Thr Ala Ile Asn Asn Thr  
 1265 1270 1275 1280  
 Pro Arg Asn Ile Gly Lys Asp Gly Lys Phe Gln Met Leu Val Cys Leu  
 1285 1290 1295  
 Gly Ala Arg Asp His Leu Leu His His Trp Ile Ala Leu Leu Ala Asp  
 1300 1305 1310  
 Cys Pro Ile Thr Ala His Met Tyr Glu Asp Val Ala Leu Ile Lys Asp  
 1315 1320 1325  
 His Thr Leu Val Asn Ser Leu Ile Arg Val Leu Gln Thr Leu Gln  
 1330 1335 1340 1343

<210> 424  
 <211> 556  
 <212> PRT  
 <213> Homo sapiens

<400> 424  
 Leu Ala Asp Gly Asp Met Leu Pro Leu Leu Leu Leu Pro Leu Leu Trp  
 1 5 10 15  
 Gly Gly Ser Leu Gln Glu Lys Pro Val Tyr Glu Leu Gln Val Gln Lys  
 20 25 30  
 Ser Val Thr Val Gln Glu Gly Leu Cys Val Leu Val Pro Cys Ser Phe  
 35 40 45  
 Ser Tyr Pro Trp Arg Ser Trp Tyr Ser Ser Pro Pro Leu Tyr Val Tyr  
 50 55 60  
 Trp Phe Arg Asp Gly Glu Ile Pro Tyr Tyr Ala Glu Val Val Ala Thr  
 65 70 75 80  
 Asn Asn Pro Asp Arg Arg Val Lys Pro Glu Thr Gln Gly Arg Phe Arg  
 85 90 95  
 Leu Leu Gly Asp Val Gln Lys Lys Asn Cys Ser Leu Ser Ile Gly Asp  
 100 105 110  
 Ala Arg Met Glu Asp Thr Gly Ser Tyr Phe Phe Arg Val Glu Arg Gly  
 115 120 125  
 Arg Asp Val Lys Tyr Ser Tyr Gln Gln Asn Lys Leu Asn Leu Glu Val  
 130 135 140  
 Thr Ala Leu Ile Glu Lys Pro Asp Ile His Phe Leu Glu Pro Leu Glu  
 145 150 155 160  
 Ser Gly Arg Pro Thr Arg Leu Ser Cys Ser Leu Pro Gly Ser Cys Glu  
 165 170 175  
 Ala Gly Pro Pro Leu Thr Phe Ser Trp Thr Gly Asn Ala Leu Ser Pro  
 180 185 190  
 Leu Asp Pro Glu Thr Thr Arg Ser Ser Glu Leu Thr Leu Thr Pro Arg  
 195 200 205  
 Pro Glu Asp His Gly Thr Asn Leu Thr Cys Gln Met Lys Arg Gln Gly  
 210 215 220  
 Ala Gln Val Thr Thr Glu Arg Thr Val Gln Leu Asn Val Ser Tyr Ala  
 225 230 235 240  
 Pro Gln Thr Ile Thr Ile Phe Arg Asn Gly Ile Ala Leu Glu Ile Leu  
 245 250 255  
 Gln Asn Thr Ser Tyr Leu Pro Val Leu Glu Gly Gln Ala Leu Arg Leu  
 260 265 270  
 Leu Cys Asp Ala Pro Ser Asn Pro Pro Ala His Leu Ser Trp Phe Gln  
 275 280 285  
 Gly Ser Pro Ala Leu Asn Ala Thr Pro Ile Ser Asn Thr Gly Ile Leu



```

      290              295              300
Glu Leu Arg Arg Val Arg Ser Ala Glu Glu Gly Gly Phe Thr Cys Arg
305              310              315              320
Ala Gln His Pro Leu Gly Ser Leu Gln Ile Phe Leu Asn Leu Ser Val
      325              330              335
Tyr Ser Leu Pro Gln Leu Leu Gly Pro Ser Cys Ser Trp Glu Ala Glu
      340              345              350
Gly Leu His Cys Arg Cys Ser Phe Arg Ala Arg Pro Ala Pro Ser Leu
      355              360              365
Cys Trp Arg Leu Glu Glu Lys Pro Leu Glu Gly Asn Ser Ser Gln Gly
      370              375              380
Ser Phe Lys Val Asn Ser Ser Ala Gly Pro Trp Ala Asn Ser Ser
385              390              395              400
Leu Ile Leu His Gly Gly Leu Ser Ser Asp Leu Lys Val Ser Cys Lys
      405              410              415
Ala Trp Asn Ile Tyr Gly Ser Gln Ser Gly Ser Val Leu Leu Leu Gln
      420              425              430
Gly Arg Ser Asn Leu Gly Thr Gly Val Val Pro Ala Ala Leu Gly Gly
      435              440              445
Ala Gly Val Met Ala Leu Leu Cys Ile Cys Leu Cys Leu Ile Phe Phe
      450              455              460
Leu Ile Val Lys Ala Arg Arg Lys Gln Ala Ala Gly Arg Pro Glu Lys
      465              470              475              480
Met Asp Asp Glu Asp Pro Ile Met Gly Thr Ile Thr Ser Gly Ser Arg
      485              490              495
Lys Lys Pro Trp Pro Asp Ser Pro Gly Asp Gln Ala Ser Pro Pro Gly
      500              505              510
Asp Ala Pro Pro Leu Glu Glu Gln Lys Glu Leu His Tyr Ala Ser Leu
      515              520              525
Ser Phe Ser Glu Met Lys Ser Arg Glu Pro Lys Asp Gln Glu Ala Pro
      530              535              540
Ser Thr Thr Glu Tyr Ser Glu Ile Lys Thr Ser Lys
545              550              555 556

```

```

<210> 425
<211> 114
<212> PRT
<213> Homo sapiens

```

```

      <400> 425
His Ala Gly Cys Gln Phe Lys Ala Leu Leu Trp Lys Asn Trp Leu Cys
  1              5              10              15
Arg Leu Arg Asn Pro Val Leu Phe Leu Ala Glu Phe Phe Trp Pro Cys
      20              25              30
Ile Leu Phe Val Ile Leu Thr Val Leu Arg Phe Gln Glu Pro Pro Arg
      35              40              45
Tyr Arg Asp Ile Cys Tyr Leu Gln Pro Arg Asp Leu Pro Ser Cys Gly
      50              55              60
Val Ile Pro Phe Val Gln Ser Leu Leu Cys Asn Thr Gly Ser Arg Cys
      65              70              75              80
Arg Asn Ser Ala Met Lys Gly Gln Trp Ser Ile Ile Phe Gly Lys Arg
      85              90              95
Asn Thr Lys Ile Phe Phe Arg Asn Leu Arg Lys Leu Ile His Arg Thr
      100              105              110
Gly
113

```

```

<210> 426
<211> 104
<212> PRT

```

&lt;213&gt; Homo sapiens

&lt;400&gt; 426

```

Gln Tyr Asp Pro Glu Asp Lys Thr Gln Ser Glu Gln Trp Leu Pro Thr
 1           5           10           15
Gly Arg Ser Gly Pro Val Lys Ala Lys Glu Val Gln Ser Arg Ala Lys
          20           25           30
Val Met Ala Gly Val Phe Trp Asp Ala Gln Gly Asn Met Pro Ala Asp
          35           40           45
Phe Leu Glu Gly Gln Arg Thr Ile Thr Ser Ala Tyr Tyr Glu Met Thr
          50           55           60
Trp Arg Lys Leu Ala Lys Val Leu Ala Glu Lys His Pro Gly Lys Leu
          65           70           75           80
Leu Gln Arg Val Leu Leu Asn His Asp Asn Val Leu Ala His Tyr Ser
          85           90           95
His Gln Thr Arg Ala Ile Phe
          100           103

```

&lt;210&gt; 427

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(138)

&lt;223&gt; Xaa = any amino acid or nothing

&lt;400&gt; 427

```

Arg Gln Ser Ser Arg Asp His Thr Ile Pro Ser Leu Arg Val Tyr Xaa
 1           5           10           15
His Ser Glu Ser Xaa Gly Tyr Ser Val Tyr Leu Leu Lys Asn Phe Tyr
          20           25           30
Ser Met Lys Leu Ala Leu Glu Thr Thr Leu Cys Ala Leu Phe Leu Arg
          35           40           45
Leu Gln Gln Leu Leu His Gln Arg Thr His Pro Val Phe Ile Thr His
          50           55           60
Ile Arg Ala His Ser Ser Leu Pro Gly Pro Leu Ala Tyr Gly Asn Asp
          65           70           75           80
Gln Ala Ala Leu Gln Val Val Thr Ser Leu Leu Asp Gln Ala Thr Gln
          85           90           95
Leu His Gln Phe Phe Tyr Xaa Asn Xaa Gln Lys Leu Ile Leu Asn Asn
          100           105           110
Phe Asn Leu Tyr Arg Glu Leu Ala Lys Gln Ile Ile Xaa Arg Cys Pro
          115           120           125
Asp Cys Gln Leu Thr Gly Thr Ala Pro Leu
          130           135           138

```

&lt;210&gt; 428

&lt;211&gt; 791

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 428

```

Asn Ile Asn Arg Lys Leu Pro Phe Pro Pro Leu Asp Ser Gly Tyr Thr
 1           5           10           15
Leu Phe Ala Ile Cys Glu Ile Ser Pro Trp Leu Arg Asp Gly Ile Ser
          20           25           30
Glu Pro Glu Cys Ser Ser Glu Gln His Pro Glu Val Ser Ile Thr Leu

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      35      40      45
Leu Pro Val Glu Pro Met Thr Ser Asp Gln Asp Ala Lys Val Val Ala
      50      55      60
Glu Pro Gln Thr Gln Arg Val Gln Glu Gly Lys Asp Ser Ala His Leu
      65      70      75      80
Met Asn Gly Pro Ile Ser Gln Thr Thr Ser Gln Thr Ser Ser Ile Pro
      85      90      95
Pro Leu Ser Gln Val Pro Ala Thr Lys Val Ser Glu Leu Asn Pro Asn
      100      105      110
Ala Glu Val Trp Gly Ala Pro Val Leu His Leu Glu Ala Ser Ser Ala
      115      120      125
Ala Asp Gly Val Ser Ala Ala Trp Glu Glu Val Ala Gly His His Ala
      130      135      140
Asp Arg Gly Pro Gln Gly Ser Asp Ala Asn Gly Asp Gly Asp Gln Gly
      145      150      155      160
His Glu Asn Ala Ala Leu Pro Asp Pro Gln Glu Ser Asp Pro Ala Asp
      165      170      175
Met Asn Ala Leu Ala Leu Gly Pro Ser Glu Tyr Asp Ser Leu Pro Glu
      180      185      190
Asn Ser Glu Thr Gly Gly Asn Glu Ser Gln Pro Asp Ser Gln Glu Asp
      195      200      205
Pro Arg Glu Val Leu Lys Lys Thr Leu Glu Phe Cys Leu Ser Arg Glu
      210      215      220
Asn Leu Ala Ser Asp Met Tyr Leu Ile Ser Gln Met Asp Ser Asp Gln
      225      230      235      240
Tyr Val Pro Ile Thr Thr Val Ala Asn Leu Asp His Ile Lys Lys Leu
      245      250      255
Ser Thr Asp Val Asp Leu Ile Val Glu Val Leu Arg Ser Leu Pro Leu
      260      265      270
Val Gln Val Asp Glu Lys Gly Glu Lys Val Arg Pro Asn Gln Asn Arg
      275      280      285
Cys Ile Val Ile Leu Arg Glu Ile Ser Glu Ser Thr Pro Val Glu Glu
      290      295      300
Val Glu Ala Leu Phe Lys Gly Asp Asn Leu Pro Lys Phe Ile Asn Cys
      305      310      315      320
Glu Phe Ala Tyr Asn Asp Asn Trp Phe Ile Thr Phe Glu Thr Glu Ala
      325      330      335
Asp Ala Gln Gln Ala Tyr Lys Tyr Leu Arg Glu Glu Val Lys Thr Phe
      340      345      350
Gln Gly Lys Pro Ile Lys Ala Arg Ile Lys Ala Lys Ala Ile Ala Ile
      355      360      365
Asn Thr Phe Leu Pro Lys Asn Gly Phe Arg Pro Leu Asp Val Ser Leu
      370      375      380
Tyr Ala Gln Gln Arg Tyr Ala Thr Ser Phe Tyr Phe Pro Pro Met Tyr
      385      390      395      400
Ser Pro Gln Gln Gln Phe Pro Leu Tyr Ser Leu Ile Thr Pro Gln Thr
      405      410      415
Trp Ser Ala Thr His Ser Tyr Leu Asp Pro Pro Leu Val Thr Pro Phe
      420      425      430
Pro Asn Thr Gly Phe Ile Asn Gly Phe Thr Ser Pro Ala Phe Lys Pro
      435      440      445
Ala Ala Ser Pro Leu Thr Ser Leu Arg Gln Tyr Pro Pro Arg Ser Arg
      450      455      460
Asn Pro Ser Lys Ser His Leu Arg His Ala Ile Pro Ser Ala Glu Arg
      465      470      475      480
Gly Pro Gly Leu Leu Glu Ser Pro Ser Ile Phe Asn Phe Thr Ala Asp
      485      490      495
Arg Leu Ile Asn Gly Val Arg Ser Pro Gln Thr Arg Gln Ala Gly Gln
      500      505      510
Thr Arg Thr Arg Val Gln Asn Pro Ser Ala Tyr Ala Lys Arg Glu Ala
      515      520      525
Gly Pro Gly Arg Val Glu Pro Gly Ser Leu Glu Ser Ser Pro Gly Leu
      530      535      540

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Gly Arg Gly Arg Lys Asn Ser Phe Gly Tyr Arg Lys Lys Arg Glu Glu  
 545 550 555 560  
 Lys Phe Thr Ser Ser Gln Thr Gln Ser Pro Thr Pro Pro Lys Pro Pro  
 565 570 575  
 Ser Pro Ser Phe Glu Leu Gly Leu Ser Ser Phe Pro Pro Leu Pro Gly  
 580 585 590  
 Ala Ala Gly Asn Leu Lys Thr Glu Asp Leu Phe Glu Asn Arg Leu Ser  
 595 600 605  
 Ser Leu Ile Ile Gly Pro Ser Lys Glu Arg Thr Leu Ser Ala Asp Ala  
 610 615 620  
 Ser Val Asn Thr Leu Pro Val Val Val Ser Arg Glu Pro Ser Val Pro  
 625 630 635 640  
 Ala Ser Cys Ala Val Ser Ala Thr Tyr Glu Arg Ser Pro Ser Pro Ala  
 645 650 655  
 His Leu Pro Asp Asp Pro Lys Val Ala Glu Lys Gln Arg Glu Thr His  
 660 665 670  
 Ser Val Asp Arg Leu Pro Ser Ala Leu Thr Ala Thr Ala Cys Lys Ser  
 675 680 685  
 Val Gln Val Asn Gly Ala Ala Thr Glu Leu Arg Lys Pro Ser Tyr Ala  
 690 695 700  
 Glu Ile Cys Gln Arg Thr Ser Lys Glu Pro Pro Ser Ser Pro Leu Gln  
 705 710 715 720  
 Pro Gln Lys Glu Gln Lys Pro Asn Thr Val Gly Cys Gly Lys Glu Glu  
 725 730 735  
 Lys Lys Leu Ala Glu Pro Ala Glu Arg Tyr Arg Glu Pro Pro Ala Leu  
 740 745 750  
 Lys Ser Thr Pro Gly Ala Pro Arg Asp Gln Arg Arg Pro Ala Gly Gly  
 755 760 765  
 Arg Pro Ser Pro Ser Ala Met Gly Lys Arg Leu Ser Arg Glu Gln Ser  
 770 775 780  
 Thr Pro Pro Lys Ser Pro Gln  
 785 790 791

<210> 429  
 <211> 302  
 <212> PRT  
 <213> Homo sapiens

<400> 429  
 Ser Ala Ile Val Pro Gly Pro Gly Leu Glu Arg Val His Trp Gly Arg  
 1 5 10 15  
 Pro Cys Ala Pro Ala Pro Arg Lys Met Pro Asp Gln Ala Leu Gln Gln  
 20 25 30  
 Met Leu Asp Arg Ser Cys Trp Val Cys Phe Ala Thr Asp Glu Asp Asp  
 35 40 45  
 Arg Thr Ala Glu Trp Val Arg Pro Cys Arg Cys Arg Gly Ser Thr Lys  
 50 55 60  
 Trp Val His Gln Ala Cys Leu Gln Arg Trp Val Asp Glu Lys Gln Arg  
 65 70 75 80  
 Gly Asn Ser Thr Ala Arg Val Ala Cys Pro Gln Cys Asn Ala Glu Tyr  
 85 90 95  
 Leu Ile Val Phe Pro Lys Leu Gly Pro Val Val Tyr Val Leu Asp Leu  
 100 105 110  
 Ala Asp Arg Leu Ile Ser Lys Ala Cys Pro Phe Ala Ala Ala Gly Ile  
 115 120 125  
 Met Val Gly Ser Ile Tyr Trp Thr Ala Val Thr Tyr Gly Ala Val Thr  
 130 135 140  
 Val Met Gln Val Val Gly His Lys Glu Gly Leu Asp Val Met Glu Arg  
 145 150 155 160  
 Ala Asp Pro Leu Phe Leu Leu Ile Gly Leu Pro Thr Ile Pro Val Met  
 165 170 175

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Leu Ile Leu Gly Lys Met Ile Arg Trp Glu Asp Tyr Val Leu Arg Leu
      180      185      190
Trp Arg Lys Tyr Ser Asn Lys Leu Gln Ile Leu Asn Ser Ile Phe Pro
      195      200      205
Gly Ile Gly Cys Pro Val Pro Arg Ile Pro Ala Glu Ala Asn Pro Leu
      210      215      220
Ala Asp His Val Ser Ala Thr Arg Ile Leu Cys Gly Ala Leu Val Phe
      225      230      235      240
Pro Thr Ile Ala Thr Ile Val Gly Lys Leu Met Phe Ser Ser Val Asn
      245      250      255
Ser Asn Leu Gln Arg Thr Ile Leu Gly Gly Ile Ala Phe Val Ala Ile
      260      265      270
Lys Gly Ala Phe Lys Val Tyr Phe Lys Gln Gln Gln Tyr Leu Arg Gln
      275      280      285
Ala His Arg Lys Ile Leu Asn Tyr Pro Glu Gln Glu Glu Ala
      290      295      300      302

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<210> 430
<211> 111
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(109)
<223> Xaa = any amino acid or nothing

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<400> 430
Lys Ile Ser Ala Cys Phe Thr Lys Gly Ala Ala Xaa Asn Thr Gly Thr
  1           5           10           15
Ile Gln Lys Thr Ser Ala Ile Leu Gln Pro His Ala Glu Val Ser Leu
      20      25      30
Lys Lys Gly Cys Xaa Arg Lys Ser Ser Ala Xaa Ala Xaa Leu Gln Ala
      35      40      45
Met Tyr Leu Val Val Cys Ser Thr Trp Arg Glu Arg Trp Pro Glu Val
      50      55      60
Gln Ile Tyr Thr Asp Leu Xaa Val Val Thr Asn Ser Leu Ile Val Cys
      65      70      75      80
Xaa Gly Xaa Xaa Lys Lys Asn Asp Xaa Lys Ser Val Asp Lys Glu Ile
      85      90      95
Xaa Gly Thr Gly Met Xaa Thr Asp Leu Ser Asn Trp Ala
      100      105      109

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<210> 431
<211> 175
<212> PRT
<213> Homo sapiens

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<400> 431
Ala Trp Arg Ala Gly Gly Arg Arg Arg Val Gly Gln Gly Asn Ser Gly
  1           5           10           15
Leu Gln Ser Pro Cys Trp Gly Phe Gly Glu Arg Leu Asp Pro Gly Phe
      20      25      30
Trp Asp Ala Ser Gly Glu Gly Ser Thr Gly Phe Ala Phe Ile Arg Pro
      35      40      45
Lys Met Pro Phe Phe Gly Asn Thr Phe Ser Pro Lys Lys Thr Pro Pro
      50      55      60
Arg Lys Ser Ala Ser Leu Ser Asn Leu His Ser Leu Asp Arg Ser Thr
      65      70      75      80
Arg Glu Val Glu Leu Gly Leu Glu Tyr Gly Ser Pro Thr Met Asn Leu

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<210> 432
<211> 215
<212> PRT
<213> Homo sapiens
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<210> 433
<211> 324
<212> PRT
<213> Homo sapiens
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      <400> 433
Thr Ile Arg Ser Thr Thr Asp Pro Val Met Ser Gln Cys Ala Cys Leu
 1             5             10             15
Glu Glu Val His Leu Pro Asn Ile Lys Pro Gly Glu Gly Leu Gly Met
      20             25             30
Tyr Ile Lys Ser Thr Tyr Asp Gly Leu His Val Ile Thr Gly Thr Thr
      35             40             45

```

Glu Asn Ser Pro Ala Asp Arg Ser Gln Lys Ile His Ala Gly Asp Glu  
 50 55 60  
 Val Ile Gln Val Asn Gln Gln Thr Val Val Gly Trp Gln Leu Lys Asn  
 65 70 75 80  
 Leu Val Lys Lys Leu Arg Glu Asn Pro Thr Gly Val Val Leu Leu Leu  
 85 90 95  
 Lys Lys Arg Pro Thr Gly Ser Phe Asn Phe Thr Pro Ala Pro Leu Lys  
 100 105 110  
 Asn Leu Arg Trp Lys Pro Pro Leu Val Gln Thr Ser Pro Pro Pro Ala  
 115 120 125  
 Thr Thr Gln Ser Pro Glu Ser Thr Met Asp Thr Ser Leu Lys Lys Glu  
 130 135 140  
 Lys Ser Ala Ile Leu Asp Leu Tyr Ile Pro Pro Pro Ala Val Pro  
 145 150 155 160  
 Tyr Ser Pro Arg Asp Glu Asn Gly Ser Phe Val Tyr Gly Gly Ser Ser  
 165 170 175  
 Lys Cys Lys Gln Pro Leu Pro Gly Pro Lys Gly Ser Glu Ser Pro Asn  
 180 185 190  
 Ser Phe Leu Asp Gln Glu Ser Arg Arg Arg Arg Phe Thr Ile Ala Asp  
 195 200 205  
 Ser Asp Gln Leu Pro Gly Tyr Ser Val Glu Thr Asn Ile Leu Pro Thr  
 210 215 220  
 Lys Met Arg Glu Lys Thr Pro Ser Tyr Gly Lys Pro Arg Pro Leu Ser  
 225 230 235 240  
 Met Pro Ala Asp Gly Asn Trp Met Gly Ile Val Asp Pro Phe Ala Arg  
 245 250 255  
 Pro Arg Gly His Gly Arg Lys Gly Glu Asp Ala Leu Cys Arg Tyr Phe  
 260 265 270  
 Ser Asn Glu Arg Ile Pro Pro Ile Ile Glu Glu Ser Ser Ser Pro Pro  
 275 280 285  
 Tyr Arg Phe Ser Arg Pro Thr Thr Glu Arg His Leu Val Arg Gly Ala  
 290 295 300  
 Asp Tyr Ile Arg Gly Ser Arg Cys Tyr Ile Asn Ser Asp Leu His Ser  
 305 310 315 320  
 Ser Ala Thr  
 323

<210> 434  
 <211> 352  
 <212> PRT  
 <213> Homo sapiens

<400> 434  
 Pro Thr Ile Arg His Glu Gly Trp Lys Gly Cys Thr Cys Thr Phe Lys  
 1 5 10 15  
 Asp Arg Ser Lys Leu Arg Glu His Leu Arg Ser His Thr Gln Glu Lys  
 20 25 30  
 Val Val Ala Cys Pro Thr Cys Gly Gly Met Phe Ala Asn Asn Thr Lys  
 35 40 45  
 Phe Leu Asp His Ile Arg Arg Gln Thr Ser Leu Asp Gln Gln His Phe  
 50 55 60  
 Gln Cys Ser His Cys Ser Lys Arg Phe Ala Thr Glu Arg Leu Leu Arg  
 65 70 75 80  
 Asp His Met Arg Asn His Val Asn His Tyr Lys Cys Pro Leu Cys Asp  
 85 90 95  
 Met Thr Cys Pro Leu Pro Ser Ser Leu Arg Asn His Met Arg Phe Arg  
 100 105 110  
 His Ser Glu Asp Arg Pro Phe Lys Cys Asp Cys Cys Asp Tyr Ser Cys  
 115 120 125  
 Lys Asn Leu Ile Asp Leu Gln Lys His Leu Asp Thr His Ser Glu Glu  
 130 135 140

Pro Ala Tyr Arg Cys Asp Phe Glu Asn Cys Thr Phe Ser Ala Arg Ser  
 145 150 155 160  
 Leu Cys Ser Ile Lys Ser His Tyr Arg Lys Val His Glu Gly Asp Ser  
 165 170 175  
 Glu Pro Arg Tyr Lys Cys His Val Cys Asp Lys Cys Phe Thr Arg Gly  
 180 185 190  
 Asn Asn Leu Thr Val His Leu Arg Lys Lys His Gln Phe Lys Trp Pro  
 195 200 205  
 Ser Gly His Pro Arg Phe Arg Tyr Lys Glu His Glu Asp Gly Tyr Met  
 210 215 220  
 Arg Leu Gln Leu Val Arg Tyr Glu Ser Val Glu Leu Thr Gln Gln Leu  
 225 230 235 240  
 Leu Arg Gln Pro Gln Glu Gly Ser Gly Leu Gly Thr Ser Leu Asn Glu  
 245 250 255  
 Ser Ser Leu Gln Gly Ile Ile Leu Glu Thr Val Pro Gly Glu Pro Gly  
 260 265 270  
 Arg Lys Glu Glu Glu Glu Glu Gly Lys Gly Ser Glu Gly Thr Ala Leu  
 275 280 285  
 Ser Ala Ser Gln Asp Asn Pro Ser Ser Val Ile His Val Val Asn Gln  
 290 295 300  
 Thr Asn Ala Gln Gly Gln Gln Glu Ile Val Tyr Tyr Val Leu Ser Glu  
 305 310 315 320  
 Ala Pro Gly Glu Pro Pro Pro Val Pro Glu Pro Pro Ser Gly Gly Ile  
 325 330 335  
 Met Glu Lys Leu Gln Gly Ile Ala Glu Glu Pro Glu Ile Gln Met Val  
 340 345 350 352

<210> 435  
 <211> 503  
 <212> PRT  
 <213> Homo sapiens

<400> 435  
 Arg Val Trp Thr Leu Glu Trp Gly Leu Leu Phe Phe Gly Asn Leu Leu  
 1 5 10 15  
 Pro Phe Pro Gly Trp Cys Cys Gln Glu Gly Pro Ser Glu Gly Cys Asn  
 20 25 30  
 Leu Phe Leu Trp Arg Gln Val Leu Ala Trp Pro Gly Ser Ser Thr Met  
 35 40 45  
 Phe Leu Leu Leu Pro Phe Asp Ser Leu Ile Val Asn Leu Leu Gly Ile  
 50 55 60  
 Ser Leu Thr Val Leu Phe Thr Leu Leu Leu Val Phe Ile Ile Val Pro  
 65 70 75 80  
 Ala Ile Phe Gly Val Ser Phe Gly Ile Arg Lys Leu Tyr Met Lys Ser  
 85 90 95  
 Leu Leu Lys Ile Phe Ala Trp Ala Thr Leu Arg Met Glu Arg Gly Ala  
 100 105 110  
 Lys Glu Lys Asn His Gln Leu Tyr Lys Pro Tyr Thr Asn Gly Ile Ile  
 115 120 125  
 Ala Lys Asp Pro Thr Ser Leu Glu Glu Glu Ile Lys Glu Ile Arg Arg  
 130 135 140  
 Ser Gly Ser Ser Lys Ala Leu Asp Asn Thr Pro Glu Phe Glu Leu Ser  
 145 150 155 160  
 Asp Ile Phe Tyr Phe Cys Arg Lys Gly Met Glu Thr Ile Met Asp Asp  
 165 170 175  
 Glu Val Thr Lys Arg Phe Ser Ala Glu Glu Leu Glu Ser Trp Asn Leu  
 180 185 190  
 Leu Ser Arg Thr Asn Tyr Asn Phe Gln Tyr Ile Ser Leu Arg Leu Thr  
 195 200 205



Val Leu Trp Gly Leu Gly Val Leu Ile Arg Tyr Cys Phe Leu Leu Pro  
 210 215 220  
 Leu Arg Ile Ala Leu Ala Phe Thr Gly Ile Ser Leu Leu Val Val Gly  
 225 230 235 240  
 Thr Thr Val Val Gly Tyr Leu Pro Asn Gly Arg Phe Lys Glu Phe Met  
 245 250 255  
 Ser Lys His Val His Leu Met Cys Tyr Arg Ile Cys Val Arg Ala Leu  
 260 265 270  
 Thr Ala Ile Ile Thr Tyr His Asp Arg Glu Asn Arg Pro Arg Asn Gly  
 275 280 285  
 Gly Ile Cys Val Ala Asn His Thr Ser Pro Ile Asp Val Ile Ile Leu  
 290 295 300  
 Ala Ser Asp Gly Tyr Tyr Ala Met Val Gly Gln Val His Gly Gly Leu  
 305 310 315 320  
 Met Gly Val Ile Gln Arg Ala Met Val Lys Ala Cys Pro His Val Trp  
 325 330 335  
 Phe Glu Arg Ser Glu Val Lys Asp Arg His Leu Val Ala Lys Arg Leu  
 340 345 350  
 Thr Glu His Val Gln Asp Lys Ser Lys Leu Pro Ile Leu Ile Phe Pro  
 355 360 365  
 Glu Gly Thr Cys Ile Asn Asn Thr Ser Val Met Met Phe Lys Lys Gly  
 370 375 380  
 Ser Phe Glu Ile Gly Ala Thr Val Tyr Pro Val Ala Ile Lys Tyr Asp  
 385 390 395 400  
 Pro Gln Phe Gly Asp Ala Phe Trp Asn Ser Lys Tyr Gly Met Val  
 405 410 415  
 Thr Tyr Leu Leu Arg Met Met Thr Ser Trp Ala Ile Val Cys Ser Val  
 420 425 430  
 Trp Tyr Leu Pro Pro Met Thr Arg Glu Ala Asp Glu Asp Ala Val Gln  
 435 440 445  
 Phe Ala Asn Arg Val Lys Ser Ala Ile Ala Arg Gln Gly Gly Leu Val  
 450 455 460  
 Asp Leu Leu Trp Asp Gly Leu Lys Arg Glu Lys Val Lys Asp Thr  
 465 470 475 480  
 Phe Lys Glu Glu Gln Gln Lys Leu Tyr Ser Lys Met Ile Val Gly Asn  
 485 490 495  
 His Lys Asp Arg Ser Arg Ser  
 500 503

<210> 436  
 <211> 608  
 <212> PRT  
 <213> Homo sapiens

<400> 436  
 Glu Val Arg Glu Gly Gly Gly Lys Glu Glu Glu Ala Gly Ser Gly Arg  
 1 5 10 15  
 Cys Val Gly Cys Gly Leu Ala Pro Lys Gly Arg Pro Arg Arg Ala  
 20 25 30  
 Asp Pro Val Ala Ser Ala Ile Met Asp Pro Val Glu Ala Val Leu Gln  
 35 40 45  
 Glu Lys Ala Leu Lys Phe Met Asn Ser Ser Glu Arg Glu Asp Cys Asn  
 50 55 60  
 Asn Gly Glu Pro Pro Arg Lys Ile Ile Pro Glu Lys Asn Ser Leu Arg  
 65 70 75 80  
 Gln Thr Tyr Asn Ser Cys Ala Arg Leu Cys Leu Asn Gln Glu Thr Val  
 85 90 95  
 Cys Leu Ala Ser Thr Ala Met Lys Thr Glu Asn Cys Val Ala Lys Thr  
 100 105 110  
 Lys Leu Ala Asn Gly Thr Ser Ser Met Ile Val Pro Lys Gln Arg Lys  
 115 120 125

Leu Ser Ala Ser Tyr Glu Lys Glu Lys Glu Leu Cys Val Lys Tyr Phe  
 130 135 140  
 Glu Gln Trp Ser Glu Ser Asp Gln Val Glu Phe Val Glu His Leu Ile  
 145 150 155 160  
 Ser Gln Met Cys His Tyr Gln His Gly His Ile Asn Ser Tyr Leu Lys  
 165 170 175  
 Pro Met Leu Gln Arg Asp Phe Ile Thr Ala Leu Pro Ala Arg Gly Leu  
 180 185 190  
 Asp His Ile Ala Glu Asn Ile Leu Ser Tyr Leu Asp Ala Lys Ser Leu  
 195 200 205  
 Cys Ala Ala Glu Leu Val Cys Lys Glu Trp Tyr Arg Val Thr Ser Asp  
 210 215 220  
 Gly Met Leu Trp Lys Lys Leu Ile Glu Arg Met Val Arg Thr Asp Ser  
 225 230 235 240  
 Leu Trp Arg Gly Leu Ala Glu Arg Arg Gly Trp Gly Gln Tyr Leu Phe  
 245 250 255  
 Lys Asn Lys Pro Pro Asp Gly Asn Ala Pro Pro Asn Ser Phe Tyr Arg  
 260 265 270  
 Ala Leu Tyr Pro Lys Ile Ile Gln Asp Ile Glu Thr Ile Glu Ser Asn  
 275 280 285  
 Trp Arg Cys Gly Arg His Ser Leu Gln Arg Ile His Cys Arg Ser Glu  
 290 295 300  
 Thr Ser Lys Gly Val Tyr Cys Leu Gln Tyr Asp Asp Gln Lys Ile Val  
 305 310 315 320  
 Ser Gly Leu Arg Asp Asn Thr Ile Lys Ile Trp Asp Lys Asn Thr Leu  
 325 330 335  
 Glu Cys Lys Arg Ile Leu Thr Gly His Thr Gly Ser Val Leu Cys Leu  
 340 345 350  
 Gln Tyr Asp Glu Arg Val Ile Ile Thr Gly Ser Ser Asp Ser Thr Val  
 355 360 365  
 Arg Val Trp Asp Val Asn Thr Gly Glu Met Leu Asn Thr Leu Ile His  
 370 375 380  
 His Cys Glu Ala Val Leu His Leu Arg Phe Asn Asn Gly Met Met Val  
 385 390 395 400  
 Thr Cys Ser Lys Asp Arg Ser Ile Ala Val Trp Asp Met Ala Ser Pro  
 405 410 415  
 Thr Asp Ile Thr Leu Arg Arg Val Leu Val Gly His Arg Ala Ala Val  
 420 425 430  
 Asn Val Val Asp Phe Asp Asp Lys Tyr Ile Val Ser Ala Ser Gly Asp  
 435 440 445  
 Arg Thr Ile Lys Val Trp Asn Thr Ser Thr Cys Glu Phe Val Arg Thr  
 450 455 460  
 Leu Asn Gly His Lys Arg Gly Ile Ala Cys Leu Gln Tyr Arg Asp Arg  
 465 470 475 480  
 Leu Val Val Ser Gly Ser Ser Asp Asn Thr Ile Arg Leu Trp Asp Ile  
 485 490 495  
 Glu Cys Gly Ala Cys Leu Arg Val Leu Glu Gly His Glu Glu Leu Val  
 500 505 510  
 Arg Cys Ile Arg Phe Asp Asn Lys Arg Ile Val Ser Gly Ala Tyr Asp  
 515 520 525  
 Gly Lys Ile Lys Val Trp Asp Leu Val Ala Ala Leu Asp Pro Arg Ala  
 530 535 540  
 Pro Ala Gly Thr Leu Cys Leu Arg Thr Leu Val Glu His Ser Gly Arg  
 545 550 555 560  
 Val Phe Arg Leu Gln Phe Asp Glu Phe Gln Ile Val Ser Ser Ser His  
 565 570 575  
 Asp Asp Thr Ile Leu Ile Trp Asp Phe Leu Asn Asp Pro Ala Ala Gln  
 580 585 590  
 Ser Glu Pro Pro Arg Ser Pro Ser Arg Thr Tyr Thr Tyr Ile Ser Arg  
 595 600 605 608

<210> 437  
 <211> 203  
 <212> PRT  
 <213> Homo sapiens

<400> 437  
 Thr Ile Ser Ser Gly Gln Pro Ser Val Ile Ser Trp Arg Phe Pro Gly  
 1 5 10 15  
 His Gly Ser Gly Trp His Glu Tyr Val Leu Ser Cys Trp Asp Ser Trp  
 20 25 30  
 Leu Leu Asn Phe Ser Ser Phe Phe Gln Ala Gly Lys Gly Asp Val Leu  
 35 40 45  
 Gly Trp Arg Leu Gly Ala Gly His His Ile Ser Leu Arg Gly Lys Gly  
 50 55 60  
 Ser Arg Leu Lys Ser Asp Phe Ser Val Ser Thr Ile Cys Ala Ile Asp  
 65 70 75 80  
 Phe Phe Leu Met Gly Leu Ala Val Thr Phe Leu Ser Glu Thr Phe Leu  
 85 90 95  
 Ser Ser Ala Gln Lys Arg Gly Arg Gly Gly Glu Ser Asp Leu Glu Pro  
 100 105 110  
 Ile Asp Ser Trp Leu Ile Thr Gln Gly Met Ile Pro Val Ala Gln Pro  
 115 120 125  
 Ser Val Met Asp Asp Ile Glu Val Trp Leu Arg Thr Asp Leu Lys Gly  
 130 135 140  
 Asp Asp Leu Glu Glu Gly Val Thr Ser Glu Glu Phe Asp Lys Phe Leu  
 145 150 155 160  
 Glu Glu Arg Ala Lys Ala Ala Glu Met Val Pro Asp Leu Pro Ser Pro  
 165 170 175  
 Pro Met Glu Ala Pro Ala Pro Ala Ser Asn Pro Ser Gly Arg Lys Lys  
 180 185 190  
 Pro Glu Arg Ser Glu Asp Ala Leu Phe Ala Leu  
 195 200 203

<210> 438  
 <211> 430  
 <212> PRT  
 <213> Homo sapiens

<400> 438  
 Val Thr Leu Ile Lys Met Asn Ala Met Leu Glu Thr Pro Glu Leu Pro  
 1 5 10 15  
 Ala Val Phe Asp Gly Val Lys Leu Ala Val Ala Ala Val Leu Tyr  
 20 25 30  
 Val Ile Val Arg Cys Leu Asn Leu Lys Ser Pro Thr Ala Pro Pro Asp  
 35 40 45  
 Leu Tyr Phe Gln Asp Ser Gly Leu Ser Arg Phe Leu Leu Lys Ser Cys  
 50 55 60  
 Pro Leu Leu Thr Lys Glu Tyr Ile Pro Pro Leu Ile Trp Gly Lys Ser  
 65 70 75 80  
 Gly His Ile Gln Thr Ala Leu Tyr Gly Lys Met Gly Arg Val Arg Ser  
 85 90 95  
 Pro His Pro Tyr Gly His Arg Lys Phe Ile Thr Met Ser Asp Gly Ala  
 100 105 110  
 Thr Ser Thr Phe Asp Leu Phe Glu Pro Leu Ala Glu His Cys Val Gly  
 115 120 125  
 Asp Asp Ile Thr Met Val Ile Cys Pro Gly Ile Ala Asn His Ser Glu  
 130 135 140  
 Lys Gln Tyr Ile Arg Thr Phe Val Asp Tyr Ala Gln Lys Asn Gly Tyr  
 145 150 155 160

Arg Cys Ala Val Leu Asn His Leu Gly Ala Leu Pro Asn Ile Glu Leu  
 165 170 175  
 Thr Ser Pro Arg Met Phe Thr Tyr Gly Cys Thr Trp Glu Phe Gly Ala  
 180 185 190  
 Met Val Asn Tyr Ile Lys Lys Thr Tyr Pro Leu Thr Gln Leu Val Val  
 195 200 205  
 Val Gly Phe Ser Leu Gly Gly Asn Ile Val Cys Lys Tyr Leu Gly Glu  
 210 215 220  
 Thr Gln Ala Asn Gln Glu Lys Val Leu Cys Cys Val Ser Val Cys Gln  
 225 230 235 240  
 Gly Tyr Ser Ala Leu Arg Ala Gln Glu Thr Phe Met Gln Trp Asp Gln  
 245 250 255  
 Cys Arg Arg Phe Tyr Asn Phe Leu Met Ala Asp Asn Met Lys Lys Ile  
 260 265 270  
 Ile Leu Ser His Arg Gln Ala Leu Phe Gly Asp His Val Lys Lys Pro  
 275 280 285  
 Gln Ser Leu Glu Asp Thr Asp Leu Ser Arg Leu Tyr Thr Ala Thr Ser  
 290 295 300  
 Leu Met Gln Ile Asp Asp Asn Val Met Arg Lys Phe His Gly Tyr Asn  
 305 310 315 320  
 Ser Leu Lys Glu Tyr Tyr Glu Glu Glu Ser Cys Met Arg Tyr Leu His  
 325 330 335  
 Arg Ile Tyr Val Pro Leu Met Leu Val Asn Ala Ala Asp Asp Pro Leu  
 340 345 350  
 Val His Glu Ser Leu Leu Thr Ile Pro Lys Ser Leu Ser Glu Lys Arg  
 355 360 365  
 Glu Asn Val Met Phe Val Leu Pro Leu His Gly Gly His Leu Gly Phe  
 370 375 380  
 Phe Glu Gly Ser Val Leu Phe Pro Glu Pro Leu Thr Trp Met Asp Lys  
 385 390 395 400  
 Leu Val Val Glu Tyr Ala Asn Ala Ile Cys Gln Trp Glu Arg Asn Lys  
 405 410 415  
 Leu Gln Cys Ser Asp Thr Glu Gln Val Glu Ala Asp Leu Glu  
 420 425 430

<210> 439  
 <211> 229  
 <212> PRT  
 <213> Homo sapiens

<400> 439  
 Lys Thr Val Asp Met Gln Arg Leu Leu Leu Leu Pro Phe Leu Leu Leu  
 1 5 10 15  
 Gly Thr Val Ser Ala Leu His Leu Glu Asn Asp Ala Pro His Leu Glu  
 20 25 30  
 Ser Leu Glu Thr Gln Ala Asp Leu Gly Gln Asp Leu Asp Ser Ser Lys  
 35 40 45  
 Glu Gln Glu Arg Asp Leu Ala Leu Thr Glu Glu Val Ile Gln Ala Glu  
 50 55 60  
 Gly Glu Glu Val Lys Ala Ser Ala Cys Gln Asp Asn Phe Glu Asp Glu  
 65 70 75 80  
 Glu Ala Met Glu Ser Asp Pro Ala Ala Leu Asp Lys Asp Phe Gln Cys  
 85 90 95  
 Pro Arg Glu Glu Asp Ile Val Glu Val Gln Gly Ser Pro Arg Cys Lys  
 100 105 110  
 Thr Cys Arg Tyr Leu Leu Val Arg Thr Pro Lys Thr Phe Ala Glu Ala  
 115 120 125  
 Gln Asn Val Cys Ser Arg Cys Tyr Gly Gly Asn Leu Val Ser Ile His  
 130 135 140  
 Asp Phe Asn Phe Asn Tyr Arg Ile Gln Cys Cys Thr Ser Thr Val Asn  
 145 150 155 160

Gln Ala Gln Val Trp Ile Gly Gly Asn Leu Arg Gly Trp Phe Leu Trp  
 165 170 175  
 Lys Arg Phe Cys Trp Thr Asp Gly Ser His Trp Asn Phe Ala Tyr Trp  
 180 185 190  
 Ser Pro Gly Gln Pro Gly Asn Gly Gln Gly Ser Cys Val Ala Leu Cys  
 195 200 205  
 Thr Lys Gly Gly Tyr Trp Arg Arg Ala Gln Cys Asp Lys Gln Leu Pro  
 210 215 220  
 Phe Val Cys Ser Phe  
 225 229

<210> 440  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 440  
 Lys Leu Thr Glu Lys Ile Lys Glu Glu Arg Ile His Cys Asn Ser Ile  
 1 5 10 15  
 Tyr Lys Ala Ser Ile Thr Leu Leu Thr Lys Val Asp Ser Asp  
 20 25 30

<210> 441  
 <211> 321  
 <212> PRT  
 <213> Homo sapiens

<221> misc\_feature  
 <222> (1)...(319)  
 <223> Xaa = any amino acid or nothing

<400> 441  
 Phe Pro Glu Glu Pro Gln Ser Pro Ala His Pro Gly Ala Lys His Arg  
 1 5 10 15  
 Gly Thr Ser Pro Ala Gln Val Gly Leu Ser Gly Arg Gly His Pro Thr  
 20 25 30  
 Ser Ala Trp Ser Gly His Trp Gln Pro Arg Trp Arg Phe Leu Ala Gln  
 35 40 45  
 Ser Leu Arg Gly Thr Asn Gly Xaa Arg Gly Gly Arg Xaa Leu Pro Gly  
 50 55 60  
 Ser Xaa Trp Gly Gly Cys Asn Ser Arg Glu Ser Arg Gly His Gln Gly  
 65 70 75 80  
 Pro Pro Lys Ala Val Pro Gly Ala Gly Xaa Glu Lys Ser Trp Gly Ser  
 85 90 95  
 Pro Gly Gly Gly His Gly Glu Asp Gly Ile Tyr Glu Ala Thr Arg Phe  
 100 105 110  
 Pro Gly Ile Pro Gly Xaa Arg Arg Ala His Val Arg Pro Gly Pro Arg  
 115 120 125  
 Arg Glu Ala Ala Pro Pro Gly Pro Gly Val Pro Pro His Pro Pro Gly  
 130 135 140  
 Thr Lys Ser Ala Ala Ser His Gln Ser Ser Met Thr Ser Leu Glu Gly  
 145 150 155 160  
 Ser Gly Ile Ser Glu Arg Leu Pro Gln Lys Pro Leu His Arg Gly Gly  
 165 170 175  
 Gly Pro His Leu Glu Glu Thr Trp Met Ala Ser Pro Glu Thr Asp Ser  
 180 185 190  
 Gly Phe Val Gly Ser Glu Thr Ser Arg Val Ser Pro Leu Thr Gln Thr  
 195 200 205  
 Pro Glu His Arg Leu Ser His Ile Ser Thr Ala Gly Thr Leu Ala Gln

```

      210              215              220
Pro Phe Ala Ala Ser Val Pro Arg Asp Gly Ala Ser Tyr Pro Lys Ala
225              230              235              240
Arg Gly Ser Leu Ile Pro Arg Arg Ala Thr Glu Pro Ser Thr Pro Arg
      245              250              255
Ser Gln Ala Gln Arg Tyr Leu Ser Ser Pro Ser Gly Pro Leu Arg Gln
      260              265              270
Arg Ala Pro Asn Phe Ser Leu Glu Arg Thr Leu Ala Ala Glu Met Ala
      275              280              285
Val Pro Gly Ser Glu Phe Glu Gly His Lys Arg Ile Ser Glu Gln Pro
      290              295              300
Leu Pro Asn Lys Thr Ile Ser Pro Pro Pro Ala Pro Ala Pro Ala
305              310              315              319

```

```

<210> 442
<211> 110
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(108)
<223> Xaa = any amino acid or nothing

```

```

<400> 442
Val Asp Asn Ser Asn Leu Ser Leu Asn Met Ala Ser Gln Arg Lys Thr
 1              5              10              15
Asn Arg Cys Glu Arg Lys Gln Leu Thr Gly Gln Asn Thr Ala Thr Lys
      20              25              30
His Glu Pro Ala Pro Trp Asn Tyr Lys Asn Thr Tyr Gly Ser Ser Thr
      35              40              45
Ile Arg Thr Thr Lys Ala Pro Gly Glu Ser Thr Asn Ala Ala Pro His
      50              55              60
Tyr His Lys Leu Cys Ser Arg Val Ser His Ile Trp Gly Asn Arg Arg
      65              70              75              80
Gly Gln His Ile Trp Asn Ala Met Asp Lys Pro Arg Pro Xaa Lys Asn
      85              90              95
Ala Phe Met Ile Met Val Ser Pro Val Asp Ala Ala
      100              105              108

```

```

<210> 443
<211> 240
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(240)
<223> Xaa = any amino acid or nothing

```

```

<400> 443
Xaa Arg Ala Met Asn Phe Ser Ile Cys Phe Leu Glu Ile Gly Ser Ile
 1              5              10              15
Xaa Thr Gly Arg Tyr Cys Lys Thr Val Leu Cys Lys Leu Arg Ala Val
      20              25              30
Leu Xaa Ser Phe Arg Val Leu Asn Ile Thr Lys Ala Tyr Leu Val Leu
      35              40              45
Phe Ser Ser Leu Tyr Lys Asn Leu Ile Cys Ser Ser Val Arg Ser Val
      50              55              60
Pro Leu Lys Lys Phe Leu Lys Ser Leu Ser Ser Ile Leu Arg Asp Arg
      65              70              75              80

```

```

Phe Phe Lys Xaa Thr Xaa Asn Pro Arg Gly Glu Arg Glu Arg Val Leu
      85          90          95
Leu Gly Asp Phe Glu Xaa Asp Arg Phe Arg Lys Cys Leu Ser Leu Ile
      100          105          110
Pro Leu Gly Gly Glu Cys Ser Ser Asp Leu Leu Arg Thr Ser Pro Ser
      115          120          125
Leu Thr Ala Leu Pro Pro Asn Ser Ile His Cys Cys Ser Asp Pro Cys
      130          135          140
Ile Thr Ser Ile Asn Leu Glu Pro Ile Lys Leu Leu Xaa His Leu Arg
      145          150          155          160
Pro Pro Glu Ala Ser Thr His Glu Ala Asn Phe Thr Met Ala Ser Pro
      165          170          175
Leu Phe Arg Pro Ser Xaa Cys Phe Lys Lys Ile Thr Pro Ser Thr His
      180          185          190
Lys Pro Glu Lys Lys Thr Arg Thr Ser Ser Ser Phe Thr Arg Xaa Gly
      195          200          205
Lys Pro Arg Arg Asn Lys Xaa Gly Phe Ser Ala Phe Asn Gly Leu Val
      210          215          220
Phe Leu Gly Leu Lys Leu Pro Cys Pro Val Pro Leu Val Xaa Asn Pro
      225          230          235          240

```

```

<210> 444
<211> 50
<212> PRT
<213> Homo sapiens

```

```

<400> 444
Gly Gly Ser Ser Pro Gly Asn Thr Ala Gly Cys Pro Ser Gly Asn Gly
 1          5          10          15
Gly Asn Ala Ala Pro Tyr Gly Gly Ala Glu Gly Val Arg Pro Pro Pro
      20          25          30
Gly Pro Ala Pro Leu Pro Pro Gly Pro Thr Lys Pro Leu Pro Pro Ala
      35          40          45
Pro Pro
      50

```

```

<210> 445
<211> 113
<212> PRT
<213> Homo sapiens

```

```

<221> misc_feature
<222> (1)...(113)
<223> Xaa = any amino acid or nothing

```

```

<400> 445
Val Lys Met Gly His Xaa Ser Leu Asp Pro Glu Ile Pro Thr Lys Ser
 1          5          10          15
Cys Lys Ser Arg Gly Ser Gly Leu Leu Asp His Phe Lys Asn Ala Arg
      20          25          30
Glu Thr Ala Gln Ala Ile Lys Gly Met His Thr Xaa Glu Val Thr Lys
      35          40          45
Cys Leu Lys Asp Val Pro Leu Xaa Lys Gln Cys Met Pro Phe Arg Leu
      50          55          60
Gly Arg Gly Gly Ala Gly Arg Cys Thr Xaa Ala Lys Gln Trp Gly Trp
      65          70          75          80
Thr Gln Gly Trp Xaa Pro Glu Lys Ser Ala Glu Phe Leu Leu His Thr

```

85 90 95  
 Ile Lys Asn Val Glu Ser His Thr Glu Cys Glu Gly Val Asp Val Gly  
 100 105 110  
 Ser  
 113

<210> 446  
 <211> 195  
 <212> PRT  
 <213> Homo sapiens  
  
 <221> misc\_feature  
 <222> (1)...(195)  
 <223> Xaa = any amino acid or nothing

<400> 446  
 Ala Ala Ala Gln Gln Arg Ser His Pro Ala Met Ser Pro Gly Thr Pro  
 1 5 10 15  
 Gly Pro Thr Met Gly Arg Ser Gln Gly Ser Pro Met Asp Pro Met Val  
 20 25 30  
 Met Lys Arg Pro Gln Leu Tyr Gly Met Gly Ser Asn Pro His Ser Gln  
 35 40 45  
 Pro Gln Gln Ser Ser Pro Tyr Pro Gly Gly Ser Tyr Gly Pro Pro Gly  
 50 55 60  
 Pro Gln Arg Tyr Pro Ile Gly Ile Gln Gly Arg Thr Pro Gly Ala Met  
 65 70 75 80  
 Ala Gly Met Gln Tyr Pro Gln Gln Gln Met Pro Pro Gln Tyr Gly Gln  
 85 90 95  
 Gln Gly Val Ser Gly Tyr Cys Gln Gln Gly Gln Gln Pro Tyr Tyr Ser  
 100 105 110  
 Gln Gln Pro Gln Pro Pro His Leu Pro Pro Gln Ala Gln Tyr Leu Pro  
 115 120 125  
 Ser Gln Ser Gln Gln Arg Tyr Gln Pro Gln Gln Asp Met Ser Gln Glu  
 130 135 140  
 Gly Tyr Gly Thr Arg Ser Gln Pro Ser Ser Gly Pro Arg Lys Thr Xaa  
 145 150 155 160  
 Pro Gly Asp Glu Pro Arg His Pro Arg Thr Asp His Gly Gln Ile Pro  
 165 170 175  
 Gly Gln Pro Asn Gly Ser Asn Gly Asp Glu Glu Thr Ser Val Val Trp  
 180 185 190  
 His Gly Gln  
 195

<210> 447  
 <211> 187  
 <212> PRT  
 <213> Homo sapiens

<400> 447  
 Leu Leu Lys Ser Ser Glu Lys Lys Leu Gln Glu Thr Pro Thr Glu Ala  
 1 5 10 15  
 Asn His Val Gln Arg Leu Arg Gln Met Leu Ala Cys Pro Pro His Gly  
 20 25 30  
 Leu Leu Asp Arg Val Ile Thr Asn Val Thr Ile Ile Val Leu Leu Trp  
 35 40 45  
 Ala Val Val Trp Ser Ile Thr Gly Ser Glu Cys Leu Pro Gly Gly Asn  
 50 55 60  
 Leu Phe Gly Ile Ile Ile Leu Phe Tyr Cys Ala Ile Ile Gly Gly Lys  
 65 70 75 80



```

Leu Leu Gly Leu Ile Lys Leu Pro Thr Leu Pro Pro Leu Pro Ser Leu
      85                      90                      95
Leu Gly Met Leu Leu Ala Gly Phe Leu Ile Arg Asn Ile Pro Val Ile
      100                    105                    110
Asn Asp Asn Val Gln Ile Lys His Lys Trp Ser Ser Ser Leu Arg Ser
      115                    120                    125
Ile Ala Leu Ser Ile Ile Leu Val Arg Ala Gly Leu Gly Leu Asp Ser
      130                    135                    140
Lys Ala Leu Lys Lys Leu Lys Gly Val Cys Val Arg Leu Ser Met Gly
      145                    150                    155                    160
Pro Cys Ile Val Glu Ala Cys Thr Ser Ala Leu Leu Ala His Tyr Leu
      165                    170                    175
Leu Gly Leu Pro Trp Gln Trp Gly Phe Ile Leu
      180                    185                    187

```

```

<210> 448
<211> 51
<212> PRT
<213> Homo sapiens

<221> misc_feature
<222> (1)...(51)
<223> Xaa = any amino acid or nothing

```

```

<400> 448
Phe Arg Leu Leu Ile Cys Glu Ile Ser Leu Leu Tyr Phe Ser Ala Asp
 1          5          10          15
Ile Tyr Thr Phe Cys Val Tyr Val Cys Leu Ser Met Phe Xaa Ser Tyr
      20          25          30
Cys Lys Leu Ala Phe Xaa Lys Xaa Ile Leu Val Leu Asp Xaa Ser Val
      35          40          45
Leu Val *
      50

```

```

<210> 449
<211> 240
<212> PRT
<213> Homo sapiens

```

```

<400> 449
Ser Ser Ile Leu Gln Ile Tyr Asp Leu Cys Val Asp Ala Leu Ser Pro
 1          5          10          15
Thr Phe Tyr Phe Leu Leu Pro Ser Ser Lys Ile Arg Asp Val Thr Phe
      20          25          30
Leu Phe Asn Glu Glu Gly Lys Asn Ile Ile Val Ile Met Ser Ser Ala
      35          40          45
Gly Tyr Ile Tyr Thr Gln Leu Met Glu Glu Ala Ser Ser Ala Gln Gln
      50          55          60
Gly Pro Phe Tyr Val Thr Asn Val Leu Glu Ile Asn His Glu Asp Leu
      65          70          75          80
Lys Asp Ser Asn Ser Gln Val Ala Gly Gly Gly Val Ser Val Tyr Tyr
      85          90          95
Ser His Val Leu Gln Met Leu Phe Phe Ser Tyr Cys Gln Gly Lys Ser
      100          105          110
Phe Ala Ala Thr Ile Ser Arg Thr Thr Leu Glu Val Leu Gln Leu Phe
      115          120          125
Pro Ile Asn Ile Lys Ser Ser Asn Gly Gly Ser Lys Thr Ser Pro Ala
      130          135          140
Leu Cys Gln Trp Ser Glu Val Met Asn His Pro Gly Leu Val Cys Cys

```

```

145          150          155          160
Val Gln Gln Thr Thr Gly Val Pro Leu Val Val Met Val Lys Pro Asp
          165          170          175
Thr Phe Leu Ile Gln Glu Ile Lys Thr Leu Pro Ala Lys Ala Lys Ile
          180          185          190
Gln Asp Met Val Ala Ile Arg His Thr Ala Cys Asn Glu Gln Gln Arg
          195          200          205
Thr Thr Met Ile Leu Leu Cys Glu Asp Gly Ser Leu Arg Ile Tyr Met
          210          215          220
Ala Asn Val Glu Asn Thr Ser Tyr Trp Leu Gln Pro Ser Leu Gln Pro
225          230          235          240

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<210> 450  
 <211> 166  
 <212> PRT  
 <213> Homo sapiens

```

<400> 450
Thr Arg Ala Gly Val Glu Gly Ala Gly Thr Trp Gly Ala Arg Arg Val
1          5          10          15
Ala Ile Ala Gly Gly Thr Ser Gly Ala Ala Ala Thr Asp Thr Asn Ala
          20          25          30
Val Ala Thr Ser Val Ser Met Met Asp Leu Val Leu Glu Glu Asp Val
          35          40          45
Thr Val Pro Gly Thr Leu Ser Gly Cys Ser Gly Leu Val Pro Ser Val
          50          55          60
Pro Asp Asp Leu Asp Gly Ile Asn Pro Asn Ala Gly Leu Gly Asn Gly
65          70          75          80
Leu Leu Pro Asn Val Ser Glu Glu Thr Val Ser Pro Thr Arg Ala Arg
          85          90          95
Asn Met Lys Asp Phe Glu Asn Gln Ile Thr Glu Leu Lys Lys Glu Asn
          100          105          110
Phe Asn Leu Lys Leu Arg Ile Tyr Phe Leu Glu Glu Arg Met Gln Gln
          115          120          125
Glu Phe His Gly Pro Thr Glu His Ile Tyr Lys Thr Asn Ile Glu Leu
130          135          140
Lys Val Glu Val Glu Ser Leu Lys Arg Glu Leu Gln Glu Arg Glu Gln
145          150          155          160
Leu Leu Ile Lys Ala Ser
          165 166

```

<210> 451  
 <211> 199  
 <212> PRT  
 <213> Homo sapiens

```

<400> 451
Thr Asn Glu Leu Ile His Arg Pro Gln Pro Asp Ser Gln Gln Arg Phe
1          5          10          15
Val Pro Val Pro Thr Pro Ala Lys Arg Ser Ala Arg Ala Pro Ser Leu
          20          25          30
Pro Ala Gly His Leu Ala Ser Leu Pro Ala Thr Met Pro Asn Val Leu
          35          40          45
Leu Pro Pro Lys Glu Ser Asn Leu Phe Lys Arg Ile Leu Lys Cys Tyr
          50          55          60
Glu Gln Lys Gln Tyr Lys Asn Gly Leu Lys Phe Cys Lys Met Ile Leu
65          70          75          80

```

Ser Asn Pro Lys Phe Ala Glu His Gly Glu Thr Leu Ala Met Lys Gly  
                             85                            90                            95  
 Leu Thr Leu Asn Cys Leu Gly Lys Lys Glu Glu Ala Tyr Glu Phe Val  
                             100                            105                            110  
 Arg Lys Gly Leu Arg Asn Asp Val Lys Ser His Val Cys Trp His Val  
                             115                            120                            125  
 Tyr Gly Leu Leu Gln Arg Ser Asp Lys Lys Tyr Asp Glu Ala Ile Lys  
                             130                            135                            140  
 Cys Tyr Arg Asn Ala Leu Lys Leu Asp Lys Asp Asn Leu Gln Ile Leu  
 145                            150                            155                            160  
 Arg Asp Leu Ser Leu Leu Gln Ile Gln Met Arg Asp Leu Glu Gly Tyr  
                             165                            170                            175  
 Arg Glu Thr Arg Tyr Gln Leu Leu Gln Leu Arg Pro Thr Gln Arg Ala  
                             180                            185                            190  
 Ser Trp Ile Gly Tyr Ala Ile  
                             195                            199

<210> 452  
 <211> 567  
 <212> PRT  
 <213> Homo sapiens

<400> 452  
 Asp Leu Phe Ile Ile Asp Gln Ile Lys Phe Ile Met Asp Ser Leu Asn  
   1                            5                            10                            15  
 Lys Glu Pro Phe Arg Lys Asn Tyr Asn Leu Ile Thr Phe Asp Ser Leu  
                             20                            25                            30  
 Glu Pro Met Gln Leu Leu Gln Val Leu Ser Asp Val Leu Ala Glu Ile  
                             35                            40                            45  
 Asp Pro Lys Gln Leu Val Asp Ile Arg Glu Glu Met Pro Glu Gln Thr  
                             50                            55                            60  
 Ala Lys Arg Met Leu Ser Leu Leu Gly Ile Leu Lys Tyr Lys Pro Ser  
   65                            70                            75                            80  
 Gly Asn Ala Thr Asp Met Ser Thr Phe Arg Gln Gly Leu Val Ile Gly  
                             85                            90                            95  
 Ser Lys Pro Val Ile Tyr Pro Val Leu His Trp Leu Leu Gln Arg Thr  
                             100                            105                            110  
 Asn Glu Leu Lys Lys Arg Ala Tyr Leu Ala Arg Phe Leu Ile Lys Leu  
                             115                            120                            125  
 Glu Val Pro Ser Glu Phe Leu Gln Asp Glu Thr Val Ala Asp Thr Asn  
                             130                            135                            140  
 Lys Gln Tyr Glu Glu Leu Met Glu Ala Phe Lys Thr Leu His Lys Glu  
 145                            150                            155                            160  
 Tyr Glu Gln Leu Lys Ile Ser Gly Phe Ser Thr Ala Glu Ile Arg Lys  
                             165                            170                            175  
 Asp Ile Ser Ala Met Glu Glu Glu Lys Asp Gln Leu Ile Lys Arg Val  
                             180                            185                            190  
 Glu His Leu Lys Lys Arg Val Glu Thr Ala Gln Asn His Gln Trp Met  
                             195                            200                            205  
 Leu Lys Ile Ala Arg Gln Leu Arg Val Glu Lys Glu Arg Glu Glu Tyr  
                             210                            215                            220  
 Leu Ala Gln Gln Lys Gln Glu Gln Lys Asn Gln Leu Phe His Ala Val  
 225                            230                            235                            240  
 Gln Arg Leu Gln Arg Val Gln Asn Gln Leu Lys Ser Met Arg Gln Ala  
                             245                            250                            255  
 Ala Ala Asp Ala Lys Pro Glu Ser Leu Met Lys Arg Leu Glu Glu Glu  
                             260                            265                            270  
 Ile Lys Phe Asn Leu Tyr Met Gly Thr Glu Lys Phe Pro Lys Glu Leu  
                             275                            280                            285  
 Glu Asn Lys Lys Lys Glu Leu His Phe Leu Gln Lys Val Val Ser Glu  
                             290                            295                            300

Pro Ala Met Gly His Ser Asp Leu Leu Glu Leu Glu Ser Lys Ile Asn  
 305 310 315 320  
 Glu Ile Asn Thr Glu Ile Asn Gln Leu Ile Glu Lys Lys Met Met Arg  
 325 330 335  
 Asn Glu Pro Ile Glu Gly Lys Leu Ser Leu Tyr Arg Gln Gln Ala Ser  
 340 345 350  
 Ile Ile Ser Arg Lys Lys Glu Ala Lys Ala Glu Glu Leu Gln Glu Ala  
 355 360 365  
 Lys Glu Lys Leu Ala Ser Leu Glu Arg Glu Ala Ser Val Lys Arg Asn  
 370 375 380  
 Gln Thr Arg Glu Phe Asp Gly Thr Glu Val Leu Lys Gly Asp Glu Phe  
 385 390 395 400  
 Lys Arg Tyr Val Asn Lys Leu Arg Ser Lys Ser Thr Val Phe Lys Lys  
 405 410 415  
 Lys His Gln Ile Ile Ala Glu Leu Lys Ala Glu Phe Gly Leu Leu Gln  
 420 425 430  
 Arg Thr Glu Glu Leu Leu Lys Gln Arg His Glu Asn Ile Gln Gln Gln  
 435 440 445  
 Leu Gln Thr Met Glu Glu Lys Lys Gly Ile Ser Gly Tyr Ser Tyr Thr  
 450 455 460  
 Gln Glu Glu Leu Glu Arg Val Ser Ala Leu Lys Ser Glu Val Asp Glu  
 465 470 475 480  
 Met Lys Gly Arg Thr Leu Asp Asp Met Ser Glu Met Val Lys Lys Leu  
 485 490 495  
 Tyr Ser Leu Val Ser Glu Lys Lys Ser Ala Leu Ala Ser Val Ile Lys  
 500 505 510  
 Glu Leu Arg Gln Leu Arg Gln Lys Tyr Gln Glu Leu Thr Gln Glu Cys  
 515 520 525  
 Asp Glu Lys Lys Ser Gln Tyr Asp Ser Cys Ala Ala Gly Leu Glu Ser  
 530 535 540  
 Asn Arg Ser Lys Leu Glu Gln Glu Val Arg Arg Leu Arg Glu Glu Cys  
 545 550 555 560  
 Leu Gln Glu Glu Ser Arg Tyr  
 565 567

<210> 453  
 <211> 1748  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (189)..(506)

<400> 453  
 aattggaagc cttgagttga gaccogtgtt gcagggtcga cccacgcgtg cgcccacgcg 60  
 tccggtgagc ttcctggagc ccagagatga gaagataaag atgccgctcc tacgaggact 120  
 gctgtggctc caggtgctgt gtgcgggccc tctccataca gaggctgtgg tacttctggt 180  
 tccttctg atg atg ggc gtg ctt ttc tgc tgc gga gcc ggc ttc ttc atc 230  
 Met Met Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe Ile  
 1 5 10  
 cgg agg cgc atg tac ccc ccg ccg ctg atc gag gag cca gcc ttc aat 278  
 Arg Arg Arg Met Tyr Pro Pro Pro Leu Ile Glu Glu Pro Ala Phe Asn  
 15 20 25 30  
 gtg tcc tac acc agg cag ccc cca aat ccc ggc cca gga gcc cag cag 326  
 Val Ser Tyr Thr Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln Gln  
 35 40 45

ccg ggg ccg ccc tat tac acc gac cca gga gga ccg ggg atg aac cct	374
Pro Gly Pro Pro Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn Pro	
50 55 60	
gtc ggg aat tcc atg gca atg gct ttc cag gtc cca ccc aac tca ccc	422
Val Gly Asn Ser Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser Pro	
65 70 75	
cag ggg agt gtg gcc tgc ccg ccc cct cca gcc tac tgc aac acg cct	470
Gln Gly Ser Val Ala Cys Pro Pro Pro Pro Ala Tyr Cys Asn Thr Pro	
80 85 90	
ccg ccc ccg tac gaa cag gta gtg aag gcc aag tag tggg gtgccccagt	520
Pro Pro Pro Tyr Glu Gln Val Val Lys Ala Lys *	
95 100 105	
gcaagaggag agacaggaga gggcctttcc ctggcctttc tgtcttcgtt gatgttcact	580
tccaggaacg gtctcgtggg ctgctaaggg cagttcctct gatatacctca cagcaagcac	640
agctctcttt caggcctttcc atggagtaca atatatgaac tcacactttg tctcctctgt	700
tgtctctgtt tctgacgcag tctgtgctct cacatggtag tgtggtgaca gtccccgagg	760
gtgacgtcc ttacggtggc gtgaccagat ctacaggaga gagactgaga ggaagaaggc	820
agtgtgggag gtgcaggtgg catgtagagg ggccaggccg agcatcccag gcaagcatcc	880
ttctgccccg gtattaatag gaagcccat gccgggcggc tcagccgatg aagcagcagc	940
cgactgagct gagcccagca ggtcatctgc tccagcctgt cctctcgtca gccttcctct	1000
tccagaagct gttggagaga cattcaggag agagcaagcc ccttgtcatg tttctgtctc	1060
tgttcatatc ctaaagatag acttctcctg caccgccagg gaagggtagc acgtgcagct	1120
ctcaccgcag gatggggcct agaatcaggc ttgccttga ggcctgacag tgatctgaca	1180
tccactaagc aaatttatatt aaattcatgg gaaatcactt cctgccccaa actgagacat	1240
tgcattttgt gagctcttgg tctgatttgg agaaaggact gttaccatt tttttggtgt	1300
gtttatggaa gtgcatgtag agcgtcctgc cctttgaaat cagactgggt gtgtgtcttc	1360
cctggacatc actgcctctc cagggcattc tcaggcccgg gggctctcctt cctcaggca	1420
gctccagtgg tgggttctga aggggtcttt caaacgggg cacatctggc tgggaagtca	1480
catggaactct tccagggaga gagaccagct gaggcgtctc tctctgaggt tgtgttgggt	1540
ctaagcgggt gtgtgctggg ctccaaggag gaggagcttg ctgggaaaag acaggagaag	1600
tactgactca actgcactga ccatgttgtc ataattagaa taaagaagaa gtggtcggaa	1660
atgcacattc ctggatagga atcacagctc accccaggat ctacaggta gtctcctgag	1720
tagttgacgg ctagcggggg agctagtt	1748

<211> 5201  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (847) .. (3063)

<400> 454  
 attttttcact tgtgatgtca tgttggtgct caaaaagttt tagatttttg aggatttcag 60  
 atttcagatt ttcagattag tgctgctcag cttgtattct gtcagtgttg cgtgtcaagg 120  
 ttttttttta acaaaatcaa tttatgtatc atttcatggt tctctgactc attgttaggg 180  
 acaaatatgc cttcccatgt gagccgcaca ggattaaagc agctccgagc tgcttcccag 240  
 ctctgacatt ttgccattct aaaaaatgag ttactcacc acttccccat cttactcttt 300  
 gagtattatg tattttcaat tgaaaactgt agttttgtga tgatgaattg gaaagctcaa 360  
 tagaacatga tctgtattcc ttgaagaaat gcaggatcca ctggaaatga ggtggagaga 420  
 gaccttttcc acccatcaga gtgaagcggg gtactctaca aggtgcattc ctgacgagga 480  
 aggccctgtg tgctgtgctg ccaattctgg cttttcctca gttcaggtgt atgcccatgc 540  
 tactacgttt gtccatcagc atttttgttt tggtttgttt tcagatgtaa atgagaggaa 600  
 gcaaagattt ttatggagac tatcaataat ctcaagaaaa tacatattca aaatgggatt 660  
 aaagccgtgc agtaagatgg gccaccaaac ataccttggg tctgatgcac tgcaagcaag 720  
 taaccagctt ctactccag tttcaagtgg ctattatgta atataaattc aaagcacata 780  
 agtgagcctg agtgcagcag tgagcagcat cctgaggtta gcattacact tctcccagtg 840  
 gagccc atg act tct gat cag gac gct aag gtt gtg gct gaa ccg cag 888  
 Met Thr Ser Asp Gln Asp Ala Lys Val Val Ala Glu Pro Gln  
 1 5 10  
 acg cag aga gtc cag gag ggc aag gac agc gct cat ctg atg aat ggt 936  
 Thr Gln Arg Val Gln Glu Gly Lys Asp Ser Ala His Leu Met Asn Gly  
 15 20 25 30  
 cct ata tct caa acc act tct cag aca agt tcc atc cca cct ttg agt 984  
 Pro Ile Ser Gln Thr Thr Ser Gln Thr Ser Ser Ile Pro Pro Leu Ser  
 35 40 45  
 cag gta cca gca act aag gtt tca gag ctg aac cct aat gca gaa gtg 1032  
 Gln Val Pro Ala Thr Lys Val Ser Glu Leu Asn Pro Asn Ala Glu Val  
 50 55 60  
 tgg ggg gct cct gtg tta cat ctg gaa gca agc agt gct gct gac ggt 1080  
 Trp Gly Ala Pro Val Leu His Leu Glu Ala Ser Ser Ala Ala Asp Gly  
 65 70 75  
 gtg agt gct gca tgg gag gag gtg gct ggc cac cac gca gac cgt ggc 1128  
 Val Ser Ala Ala Trp Glu Glu Val Ala Gly His His Ala Asp Arg Gly  
 80 85 90  
 ccg cag gga tcg gat gcc aat ggt gat ggt gac cag ggc cat gag aat 1176  
 Pro Gln Gly Ser Asp Ala Asn Gly Asp Gly Asp Gln Gly His Glu Asn

95	100	105	110	
gcc gca ttg cca gac ccg cag gag tcg gac cca gca gac atg aac gct				1224
Ala Ala Leu Pro Asp Pro Gln Glu Ser Asp Pro Ala Asp Met Asn Ala				
115		120	125	
ctc gct ctg ggt ccc tca gaa tat gac tct ctg cct gaa aat agc gag				1272
Leu Ala Leu Gly Pro Ser Glu Tyr Asp Ser Leu Pro Glu Asn Ser Glu				
130		135	140	
aca gga gga aat gag tct caa cca gac agc cag gaa gac ccc cga gaa				1320
Thr Gly Gly Asn Glu Ser Gln Pro Asp Ser Gln Glu Asp Pro Arg Glu				
145		150	155	
gta ctt aaa aaa aca ttg gaa ttc tgc tta tct agg gag aac ctt gct				1368
Val Leu Lys Lys Thr Leu Glu Phe Cys Leu Ser Arg Glu Asn Leu Ala				
160		165	170	
agt gac atg tat ctt ata tca cag atg gat agt gac cag tat gtg cca				1416
Ser Asp Met Tyr Leu Ile Ser Gln Met Asp Ser Asp Gln Tyr Val Pro				
175		180	185	190
atc aca acg gtg gct aac ctc gac cac atc aag aag ctc agc act gat				1464
Ile Thr Thr Val Ala Asn Leu Asp His Ile Lys Lys Leu Ser Thr Asp				
195		200	205	
gtg gac ttg att gtg gaa gtg cta aga tct tta cct tta gtc caa gtg				1512
Val Asp Leu Ile Val Glu Val Leu Arg Ser Leu Pro Leu Val Gln Val				
210		215	220	
gat gaa aag gga gaa aaa gta agg cca aat caa aat cgc tgc ata gta				1560
Asp Glu Lys Gly Glu Lys Val Arg Pro Asn Gln Asn Arg Cys Ile Val				
225		230	235	
ata ttg cgt gaa ata tct gaa tct acc ccc gtg gaa gaa gta gaa gca				1608
Ile Leu Arg Glu Ile Ser Glu Ser Thr Pro Val Glu Glu Val Glu Ala				
240		245	250	
cta ttt aaa gga gat aat tta cca aaa ttt ata aac tgt gaa ttt gca				1656
Leu Phe Lys Gly Asp Asn Leu Pro Lys Phe Ile Asn Cys Glu Phe Ala				
255		260	265	270
tat aat gat aat tgg ttt att aca ttt gaa aca gaa gct gat gca caa				1704
Tyr Asn Asp Asn Trp Phe Ile Thr Phe Glu Thr Glu Ala Asp Ala Gln				
275		280	285	
cag gct tac aaa tac ctt cga gaa gaa gtc aaa act ttt caa gga aaa				1752
Gln Ala Tyr Lys Tyr Leu Arg Glu Glu Val Lys Thr Phe Gln Gly Lys				
290		295	300	
cca att aag gca cgg ata aaa gca aag gca ata gct ata aac aca ttt				1800
Pro Ile Lys Ala Arg Ile Lys Ala Lys Ala Ile Ala Ile Asn Thr Phe				
305		310	315	
ttg cca aag aat gga ttt aga ccc ctg gac gtg agc ctg tat gcc cag				1848
Leu Pro Lys Asn Gly Phe Arg Pro Leu Asp Val Ser Leu Tyr Ala Gln				
320		325	330	
cag cgc tac gcg acg tcg ttc tac ttc cct ccc atg tac agc ccc cag				1896
Gln Arg Tyr Ala Thr Ser Phe Tyr Phe Pro Pro Met Tyr Ser Pro Gln				
335		340	345	350
cag cag ttc ccc ctg tac agc ctg atc act ccc cag acg tgg tca gca				1944

Gln Gln Phe Pro Leu Tyr Ser Leu Ile Thr Pro Gln Thr Trp Ser Ala	
355 360 365	
acg cac agc tat ctt gac cca ccc ttg gta act cca ttt cca aat act	1992
Thr His Ser Tyr Leu Asp Pro Pro Leu Val Thr Pro Phe Pro Asn Thr	
370 375 380	
gga ttt ata aat ggg ttt acg tct cca gcg ttc aag cct gcg gcg tct	2040
Gly Phe Ile Asn Gly Phe Thr Ser Pro Ala Phe Lys Pro Ala Ala Ser	
385 390 395	
cct ctg act tct ctc aga cag tat cct cct cga agc agg aat cct agt	2088
Pro Leu Thr Ser Leu Arg Gln Tyr Pro Pro Arg Ser Arg Asn Pro Ser	
400 405 410	
aaa tct cat ctg cgg cat gcg att cct agt gca gag agg gga cct ggg	2136
Lys Ser His Leu Arg His Ala Ile Pro Ser Ala Glu Arg Gly Pro Gly	
415 420 425 430	
tta tta gaa agt cct tca ata ttt aac ttc act gca gat cga tta att	2184
Leu Leu Glu Ser Pro Ser Ile Phe Asn Phe Thr Ala Asp Arg Leu Ile	
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Asn Gly Val Arg Ser Pro Gln Thr Arg Gln Ala Gly Gln Thr Arg Thr	
450 455 460	
cgg att caa aac cct tca gca tat gcc aag aga gag gct ggg cct ggg	2280
Arg Ile Gln Asn Pro Ser Ala Tyr Ala Lys Arg Glu Ala Gly Pro Gly	
465 470 475	
cgt gtg gag cca ggc agt ctc gaa tcc tct cct ggt tta ggg agg gga	2328
Arg Val Glu Pro Gly Ser Leu Glu Ser Ser Pro Gly Leu Gly Arg Gly	
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agg aag aat tcc ttt ggc tac cgg aag aaa agg gag gag aag ttt aca	2376
Arg Lys Asn Ser Phe Gly Tyr Arg Lys Lys Arg Glu Glu Lys Phe Thr	
495 500 505 510	
agc agc cag aca cag tct cca acg cca cca aag cct ccg tcg cca agc	2424
Ser Ser Gln Thr Gln Ser Pro Thr Pro Pro Lys Pro Pro Ser Pro Ser	
515 520 525	
ttc gag ctg ggg ctg tcc agc ttc cct cca tta cct gga gct gcc ggc	2472
Phe Glu Leu Gly Leu Ser Ser Phe Pro Pro Leu Pro Gly Ala Ala Gly	
530 535 540	
aat ttg aag aca gag gac ttg ttt gaa aac agg cta tct agc ttg ata	2520
Asn Leu Lys Thr Glu Asp Leu Phe Glu Asn Arg Leu Ser Ser Leu Ile	
545 550 555	
ata gga cca tcc aaa gaa agg acc ctc agt gca gac gca agc gtg aac	2568
Ile Gly Pro Ser Lys Glu Arg Thr Leu Ser Ala Asp Ala Ser Val Asn	
560 565 570	
acc ctt cct gta gtg gtc tcc aga gag ccc tcg gtg ccg gct tct tgt	2616
Thr Leu Pro Val Val Ser Arg Glu Pro Ser Val Pro Ala Ser Cys	
575 580 585 590	
gct gta tca gca acg tac gag cga tcc ccc tcc cca gct cat tta ccc	2664
Ala Val Ser Ala Thr Tyr Glu Arg Ser Pro Ser Pro Ala His Leu Pro	
595 600 605	



gat gat ccc aag gtg gcg gag aaa cag agg gaa acc cac agt gtg gac Asp Asp Pro Lys Val Ala Glu Lys Gln Arg Glu Thr His Ser Val Asp 610 615 620	2712
aga ctt cct tcc gcc ctc act gcg acc gcg tgt aaa tcg gtg cag gtg Arg Leu Pro Ser Ala Leu Thr Ala Thr Ala Cys Lys Ser Val Gln Val 625 630 635	2760
aac gga gcc gcc acg gaa ttg cga aag ccc agc tac gca gag att tgt Asn Gly Ala Ala Thr Glu Leu Arg Lys Pro Ser Tyr Ala Glu Ile Cys 640 645 650	2808
cag aga acg agt aaa gag cct cct tct tcc cca ttg caa ccc caa aaa Gln Arg Thr Ser Lys Glu Pro Pro Ser Ser Pro Leu Gln Pro Gln Lys 655 660 665 670	2856
gaa caa aag cca aac act gtt ggt tgt ggg aag gag gaa aag aag ctg Glu Gln Lys Pro Asn Thr Val Gly Cys Gly Lys Glu Glu Lys Lys Leu 675 680 685	2904
gca gag ccc gca gag aga tac cgg gag ccc cca gcc ctc aag tcc aca Ala Glu Pro Ala Glu Arg Tyr Arg Glu Pro Pro Ala Leu Lys Ser Thr 690 695 700	2952
cct gga gcc ccc aga gac cag agg cgg ccg gcg ggg ggc cgg ccc tcg Pro Gly Ala Pro Arg Asp Gln Arg Arg Pro Ala Gly Gly Arg Pro Ser 705 710 715	3000
ccc tcg gcc atg ggg aag cgt ctc agc cga gag cag agc act ccc ccc Pro Ser Ala Met Gly Lys Arg Leu Ser Arg Glu Gln Ser Thr Pro Pro 720 725 730	3048
aag tct cct cag tga aaaccgtacg tctgggaggg gtcgcagagc gctgtgttaa Lys Ser Pro Gln *	3103
735	
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catgttacca gaagttgtac catgatgttg ttttgacccc tgtgagctga tggccccggc	3883
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cagttgccat tattcaaata cagagaaata gccacagggc tagtggtttt caaatgcatt 5143
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<210> 455
<211> 779
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS
<222> (275)..(637)

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<220>
<221> misc_feature
<222> (1)...(779)
<223> n = a,t,c or g

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<400> 455
tgtaactggc cgaattcccg ggnccagcat ttcgtctggg caaccttctg tgatctcctg 60

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gagatttcca gggcacggta gtggttggca tgagtatgtg ttatcctgtt gggagtcttg      120
gttactaaac ttttcttctt ttttccaggc aggtaagggg gacgtgctgg ggtggaggtt      180
gggagcaggg catcacattt ccttacgtgg caaaggatca cgtctgaaga gtgacttttc      240
tgtttccaca atatgtgcta ttgacttctt tctc      atg ggt ctt gct gtg act      292
                                         Met Gly Leu Ala Val Thr
                                         1              5

ttt ctt tct gag act ttt ctg tcc tcg gcc cag aag aga ggt aga ggt      340
Phe Leu Ser Glu Thr Phe Leu Ser Ser Ala Gln Lys Arg Gly Arg Gly
              10              15              20

ggg gag tct gac ctg gag ccc ata gac agc tgg ctt ata acc cca gga      388
Gly Glu Ser Asp Leu Glu Pro Ile Asp Ser Trp Leu Ile Thr Pro Gly
              25              30              35

atg atc ccc gtt gcg cag cca tct gtc atg gac gac att gag gtg tgg      436
Met Ile Pro Val Ala Gln Pro Ser Val Met Asp Asp Ile Glu Val Trp
              40              45              50

ctc agg acc gac ctg aag ggt gat gat ctg gag gag ggt gtc aca agt      484
Leu Arg Thr Asp Leu Lys Gly Asp Asp Leu Glu Glu Gly Val Thr Ser
              55              60              65              70

gaa gag ttt gat aaa ttc ctt gaa gaa aga gcc aaa gct gct gaa atg      532
Glu Glu Phe Asp Lys Phe Leu Glu Glu Arg Ala Lys Ala Ala Glu Met
              75              80              85

gtt ccc gac ctc ccc tcg ccc ccc atg gag gct cct gcc cca gcc tca      580
Val Pro Asp Leu Pro Ser Pro Pro Met Glu Ala Pro Ala Pro Ala Ser
              90              95              100

aac cct tct ggc cgg aag aag cca gag cgg tca gag gat gcc ctc ttc      628
Asn Pro Ser Gly Arg Lys Lys Pro Glu Arg Ser Glu Asp Ala Leu Phe
              105              110              115

gcc ctg tga gcagctc tgtggtttgc ctcccagat ggcgggtccc cgcttgacc      684
Ala Leu *
              120

ccgtggacac cgggcactgg ccactcctac atcccagca ctgtattgcg gccgtctag      744

aggatccaag cttacgtacg cgggcattca cgtct      779

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<210> 456  
 <211> 1923  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (112)..(1233)

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tgttttctgta acagcagaaa gtgcactcac taggagtagt cagaattcaa a atg ctg      117
                                         Met Leu

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aag aga aag cca tcc aat gtt tca gag aag gag aaa cat caa aaa cca Lys Arg Lys Pro Ser Asn Val Ser Glu Lys Glu Lys His Gln Lys Pro 5 10 15	165
aag cga agc agc agt ttt ggg aat ttc gat cgt ttt cgg aat aat tct Lys Arg Ser Ser Ser Phe Gly Asn Phe Asp Arg Phe Arg Asn Asn Ser 20 25 30	213
tta tca aaa cca gat gat tca act gag gca cat gaa gga gat ccc aca Leu Ser Lys Pro Asp Asp Ser Thr Glu Ala His Glu Gly Asp Pro Thr 35 40 45 50	261
aat gga agt gga gaa caa agt aaa act tca aat aat gga ggc ggt ttg Asn Gly Ser Gly Glu Gln Ser Lys Thr Ser Asn Asn Gly Gly Gly Leu 55 60 65	309
ggt aaa aaa atg aga gct att tca tgg aca atg aag aaa aaa gtg ggt Gly Lys Lys Met Arg Ala Ile Ser Trp Thr Met Lys Lys Lys Val Gly 70 75 80	357
aaa aag tac atc aaa gcc ctt tct gag gaa aag gat gag gaa gat gga Lys Lys Tyr Ile Lys Ala Leu Ser Glu Glu Lys Asp Glu Glu Asp Gly 85 90 95	405
gag aat gcc cac cca tat aga aac agt gac cct gtg att ggg acc cac Glu Asn Ala His Pro Tyr Arg Asn Ser Asp Pro Val Ile Gly Thr His 100 105 110	453
aca gag aag gtg tcc ctc aaa gcc agt gac tcc atg gat agt ctc tac Thr Glu Lys Val Ser Leu Lys Ala Ser Asp Ser Met Asp Ser Leu Tyr 115 120 125 130	501
agt gga cag agc tca tca agt ggc ata aca agc tgt tca gat ggt aca Ser Gly Gln Ser Ser Ser Ser Gly Ile Thr Ser Cys Ser Asp Gly Thr 135 140 145	549
agt aac cgg gac agc ttt cga ctg gat gac gat ggc ccc tat tca gga Ser Asn Arg Asp Ser Phe Arg Leu Asp Asp Asp Gly Pro Tyr Ser Gly 150 155 160	597
cca ttc tgt ggc cgt gcc aga gtg cat acg gat ttc acg cca agt ccc Pro Phe Cys Gly Arg Ala Arg Val His Thr Asp Phe Thr Pro Ser Pro 165 170 175	645
tat gac act gac tcc ctc aaa atc aag aaa gga gac atc ata gac att Tyr Asp Thr Asp Ser Leu Lys Ile Lys Lys Gly Asp Ile Ile Asp Ile 180 185 190	693
att tgc aaa aca cca atg ggg atg tgg aca gga atg ttg aac aat aaa Ile Cys Lys Thr Pro Met Gly Met Trp Thr Gly Met Leu Asn Asn Lys 195 200 205 210	741
gtg gga aac ttc aaa ttc att tat gtg gat gtc atc tca gaa gag gaa Val Gly Asn Phe Lys Phe Ile Tyr Val Asp Val Ile Ser Glu Glu Glu 215 220 225	789
gca gcc ccc aag aaa ata aag gca aac cga agg agt aac agc aaa aaa Ala Ala Pro Lys Lys Ile Lys Ala Asn Arg Arg Ser Asn Ser Lys Lys 230 235 240	837
tcc aag act ctg cag gag ttc cta gag agg att cat ctg cag gaa tac	885

Ser Lys Thr Leu Gln Glu Phe Leu Glu Arg Ile His Leu Gln Glu Tyr	
245 250 255	
acc tca aca ctt ttg ctc aat ggt tat gag act cta gaa gat tta aaa	933
Thr Ser Thr Leu Leu Leu Asn Gly Tyr Glu Thr Leu Glu Asp Leu Lys	
260 265 270	
gat ata aaa gag agt cac ctc att gaa tta aat att gaa aac cca gat	981
Asp Ile Lys Glu Ser His Leu Ile Glu Leu Asn Ile Glu Asn Pro Asp	
275 280 285 290	
gac aga aga agg tta cta tca gct gct gaa aac ttc ctt gaa gaa gaa	1029
Asp Arg Arg Arg Leu Leu Ser Ala Ala Glu Asn Phe Leu Glu Glu Glu	
295 300 305	
att att caa gag caa gaa aat gaa cct gag ccc cta tcc ttg agc tca	1077
Ile Ile Gln Glu Gln Glu Asn Glu Pro Glu Pro Leu Ser Leu Ser Ser	
310 315 320	
gac atc tcc tta aat aag tca cag tta gat gac tgc cca agg gac tct	1125
Asp Ile Ser Leu Asn Lys Ser Gln Leu Asp Asp Cys Pro Arg Asp Ser	
325 330 335	
ggt tgc tat atc tca tca gga aat tca gat aat ggc aaa gag gat ctg	1173
Gly Cys Tyr Ile Ser Ser Gly Asn Ser Asp Asn Gly Lys Glu Asp Leu	
340 345 350	
gag tct gaa aat ctg tct gac atg gta cat aag att att atc aca gag	1221
Glu Ser Glu Asn Leu Ser Asp Met Val His Lys Ile Ile Ile Thr Glu	
355 360 365 370	
cca agt gac tga aca cgcattccca actatatatc tacagatgca ttccatttta	1276
Pro Ser Asp *	
actcttcttg agctaaaacg tcaaatagga gaggaagata agataaatat ttgtaaataa	1336
aacctaaagt ttaaatgttt taatctgaat aattgtacat aaaattttgt atctctaaca	1396
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caattgtaat aattgtggaa atgtttgtc tttaagtga aatattttta aatttgacat	1876
accctaattg taataataaa aagaactatt tgcataaaaa aaaaaaa	1923

<210> 457  
 <211> 1593  
 <212> DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (151)..(1437)

&lt;400&gt; 457

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gtgtcagtca aagcagcctc tgaacttctc      atg aaa ctc tca gcg gaa agc      171
                                   Met Lys Leu Ser Ala Glu Ser
                                   1                               5

tac aag gaa aca cag atg gtg aag att aaa gag gaa ccc atg gag gtt      219
Tyr Lys Glu Thr Gln Met Val Lys Ile Lys Glu Glu Pro Met Glu Val
      10                               15                               20

gac atc cag gac tcc cat gtc tcg ata tca ccc agc cgg aat gtt ggc      267
Asp Ile Gln Asp Ser His Val Ser Ile Ser Pro Ser Arg Asn Val Gly
      25                               30                               35

tac agc act tta atc ggg cga gag aaa acc gaa ccc tta cag aag atg      315
Tyr Ser Thr Leu Ile Gly Arg Glu Lys Thr Glu Pro Leu Gln Lys Met
      40                               45                               50                               55

cca gag ggc aga gta ccc cca gag aga aac ctc ttc agt cag gat atc      363
Pro Glu Gly Arg Val Pro Pro Glu Arg Asn Leu Phe Ser Gln Asp Ile
      60                               65                               70

tct gtg aaa atg gct tcc gag ctc ctc ttt caa ctg tca gaa aaa gtg      411
Ser Val Lys Met Ala Ser Glu Leu Leu Phe Gln Leu Ser Glu Lys Val
      75                               80                               85

agc aaa gag cac aat cat aca aaa gaa aac acc atc cgg acc acg acc      459
Ser Lys Glu His Asn His Thr Lys Glu Asn Thr Ile Arg Thr Thr Thr
      90                               95                               100

agc cct ttc ttt tca gaa gac aca ttt aga caa tca cca ttc acc tcc      507
Ser Pro Phe Phe Ser Glu Asp Thr Phe Arg Gln Ser Pro Phe Thr Ser
      105                               110                               115

aat tca aaa gaa ctg ctg ccc agt gac tcc gtg ctg cac gga aga ata      555
Asn Ser Lys Glu Leu Leu Pro Ser Asp Ser Val Leu His Gly Arg Ile
      120                               125                               130                               135

tca gct cca gaa aca gaa aag ata gtc cta gag gca gga aat gga tta      603
Ser Ala Pro Glu Thr Glu Lys Ile Val Leu Glu Ala Gly Asn Gly Leu
      140                               145                               150

cca tcc tgg aaa ttc aat gac cag ctt ttt ccc tgt gac gtg tgt ggg      651
Pro Ser Trp Lys Phe Asn Asp Gln Leu Phe Pro Cys Asp Val Cys Gly
      155                               160                               165

aaa gtg ttt ggc cga cag cag aca ttg tcc cga cac ctc tcg ctg cac      699
Lys Val Phe Gly Arg Gln Gln Thr Leu Ser Arg His Leu Ser Leu His
      170                               175                               180

aca gag gaa aga aaa tac aaa tgc cac ttg tgc ccc tat gct gct aag      747
Thr Glu Glu Arg Lys Tyr Lys Cys His Leu Cys Pro Tyr Ala Ala Lys
      185                               190                               195

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tgc cgt gca aat ctg aac cag cac ttg acc gtc cat tcc gtg aag ctg Cys Arg Ala Asn Leu Asn Gln His Leu Thr Val His Ser Val Lys Leu 200 205 210 215	795
gtg agt aca gac acc gag gac att gtc agc gcc gtc acc tct gaa ggc Val Ser Thr Asp Thr Glu Asp Ile Val Ser Ala Val Thr Ser Glu Gly 220 225 230	843
agt gat ggg aag aaa cat cct tat tat tac agt tgt cac gtg tgt gga Ser Asp Gly Lys Lys His Pro Tyr Tyr Tyr Ser Cys His Val Cys Gly 235 240 245	891
ttt gag acc gag ctc aat gtc cag ttt gtc agc cac atg tca ctc cac Phe Glu Thr Glu Leu Asn Val Gln Phe Val Ser His Met Ser Leu His 250 255 260	939
gtg gac aag gag cag tgg atg ttt tcg atc tgc tgc act gcc tgc gac Val Asp Lys Glu Gln Trp Met Phe Ser Ile Cys Cys Thr Ala Cys Asp 265 270 275	987
ttc gtc acc atg gag gaa gca gag ata aag act cac att ggc acc aag Phe Val Thr Met Glu Glu Ala Glu Ile Lys Thr His Ile Gly Thr Lys 280 285 290 295	1035
cac aca ggg gaa gac agg aag acc ccc agc gaa tca aat agc ccc tct His Thr Gly Glu Asp Arg Lys Thr Pro Ser Glu Ser Asn Ser Pro Ser 300 305 310	1083
tca tcc tcc ctc tca gct ctg agt gat tca gcc aac agc aaa gat gat Ser Ser Ser Leu Ser Ala Leu Ser Asp Ser Ala Asn Ser Lys Asp Asp 315 320 325	1131
tca gat ggc tcc cag aaa aac aag ggc ggg aac aat ctg ctg gtc atc Ser Asp Gly Ser Gln Lys Asn Lys Gly Gly Asn Asn Leu Leu Val Ile 330 335 340	1179
tct gtc atg cct ggg agc cag ccc tca ctg aac agt gag gaa aag cca Ser Val Met Pro Gly Ser Gln Pro Ser Leu Asn Ser Glu Glu Lys Pro 345 350 355	1227
gag aaa ggg ttc gaa tgt gtt ttt tgc aac ttt gtc tgc aag acg aag Glu Lys Gly Phe Glu Cys Val Phe Cys Asn Phe Val Cys Lys Thr Lys 360 365 370 375	1275
aac atg ttt gag cgt cat ctg cag ata cac ctc atc acc cgg atg ttt Asn Met Phe Glu Arg His Leu Gln Ile His Leu Ile Thr Arg Met Phe 380 385 390	1323
gag tgt gat gtg tgc cac aag ttc atg aag acc ccc gaa cag ctg ctg Glu Cys Asp Val Cys His Lys Phe Met Lys Thr Pro Glu Gln Leu Leu 395 400 405	1371
gag cat aag aaa tgc cac act gtc ccc acc ggt ggg ctc aat tta tgt Glu His Lys Lys Cys His Thr Val Pro Thr Gly Gly Leu Asn Leu Cys 410 415 420	1419
tct agg atg acc aag tag aagaat actttgaaaa aattgataat gccttctggc Ser Arg Met Thr Lys * 425	1473
tatacagtgc ccattctgca ttattccac caaccgcccc gctgccatgg agtgccacct	1533
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                                   Met Gly Ser
                                   1

cgc cac ttc gag ggg att tat gac cac gtg ggg cac ttc ggc aga ttc      163
Arg His Phe Glu Gly Ile Tyr Asp His Val Gly His Phe Gly Arg Phe
      5                      10                      15

cag aga gtc ctc tat ttc ata tgt gcc ttc cag aac atc tct tgt ggt      211
Gln Arg Val Leu Tyr Phe Ile Cys Ala Phe Gln Asn Ile Ser Cys Gly
      20                      25                      30                      35

att cac tac ttg gct tct gtg ttc atg gga gtc acc cct cat cat gtc      259
Ile His Tyr Leu Ala Ser Val Phe Met Gly Val Thr Pro His His Val
                      40                      45                      50

tgc agg ccc cca ggc aat tgt cat ctg gac tca ttg tgg gac ttg ggg      307
Cys Arg Pro Pro Gly Asn Cys His Leu Asp Ser Leu Trp Asp Leu Gly
                      55                      60                      65

att aga gga cct gag aca aag atg ctg ctg ccc tac tgc ttg cta acg      355
Ile Arg Gly Pro Glu Thr Lys Met Leu Leu Pro Tyr Cys Leu Leu Thr
                      70                      75                      80

aag cta gga cgc cgg gtg gtc ttg tgg gcc aca agc agt agc atg ttt      403
Lys Leu Gly Arg Arg Val Val Leu Trp Ala Thr Ser Ser Ser Met Phe
                      85                      90                      95

ttg ttt gga ata gca gcg gcg ttt gca gtt gat tat tac acc ttc atg      451
Leu Phe Gly Ile Ala Ala Ala Phe Ala Val Asp Tyr Tyr Thr Phe Met
      100                      105                      110                      115

gct gct cgc ttt ttt ctt gcc atg gtt gca agt ggc tat ctt gtg gtg      499
Ala Ala Arg Phe Phe Leu Ala Met Val Ala Ser Gly Tyr Leu Val Val
                      120                      125                      130

ggg ttt gtc tat gtg atg gaa ttc att ggc atg aag tct cgg aca tgg      547
Gly Phe Val Tyr Val Met Glu Phe Ile Gly Met Lys Ser Arg Thr Trp
                      135                      140                      145

gcg tct gtc cat ttg cat tcc ttt ttt gca gtt gga acc ctg ctg gtg      595
Ala Ser Val His Leu His Ser Phe Phe Ala Val Gly Thr Leu Leu Val
                      150                      155                      160

gct ttg aca gga tac ttg gtc agg acc tgg tgg ctt tac cag atg atc      643
Ala Leu Thr Gly Tyr Leu Val Arg Thr Trp Trp Leu Tyr Gln Met Ile
      165                      170                      175

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ctc tcc aca gtg act gtc ccc ttt atc ctg tgc tgt tgg gtg ctc cca Leu Ser Thr Val Thr Val Pro Phe Ile Leu Cys Cys Trp Val Leu Pro 180 185 190 195	691
gag aca cct ttt tgg ctt ctc tca gag gga cga tat gaa gaa gca caa Glu Thr Pro Phe Trp Leu Leu Ser Glu Gly Arg Tyr Glu Glu Ala Gln 200 205 210	739
aaa ata gtt gac atc atg gcc aag tgg aac agg gca agc tcc tgt aaa Lys Ile Val Asp Ile Met Ala Lys Trp Asn Arg Ala Ser Ser Cys Lys 215 220 225	787
ctg tca gaa ctt tta tca ctg gac cta caa ggt cct gtt agt aat agc Leu Ser Glu Leu Leu Ser Leu Asp Leu Gln Gly Pro Val Ser Asn Ser 230 235 240	835
ccc act gaa gtt cag aag cac aac cta tca tat ctg ttt tat aac tgg Pro Thr Glu Val Gln Lys His Asn Leu Ser Tyr Leu Phe Tyr Asn Trp 245 250 255	883
agc att acg aaa agg aca ctt acc gtt tgg cta atc tgg ttc act gga Ser Ile Thr Lys Arg Thr Leu Thr Val Trp Leu Ile Trp Phe Thr Gly 260 265 270 275	931
agt ttg gga ttc tac tcg ttt tcc ttg aat tct gtt aac tta gga ggc Ser Leu Gly Phe Tyr Ser Phe Ser Leu Asn Ser Val Asn Leu Gly Gly 280 285 290	979
aat gaa tac tta aac ctc ttc ctc ctg ggt gta gtg gaa att ccc gcc Asn Glu Tyr Leu Asn Leu Phe Leu Leu Gly Val Val Glu Ile Pro Ala 295 300 305	1027
tac acc ttc gtg tgc atc gcc atg gac aag gtc ggg agg aga aca gtc Tyr Thr Phe Val Cys Ile Ala Met Asp Lys Val Gly Arg Arg Thr Val 310 315 320	1075
ctg gcc tac tct ctt ttc tgc agt gca ctg gcc tgt ggt gtc gtt atg Leu Ala Tyr Ser Leu Phe Cys Ser Ala Leu Ala Cys Gly Val Val Met 325 330 335	1123
gtg atc ccc cag aaa cat tat att ttg ggt gtg gtg aca gct atg gtt Val Ile Pro Gln Lys His Tyr Ile Leu Gly Val Val Thr Ala Met Val 340 345 350 355	1171
gga aaà ttt gcc atc ggg gca gca ttt ggc ctc att tat ctt tat aca Gly Lys Phe Ala Ile Gly Ala Ala Phe Gly Leu Ile Tyr Leu Tyr Thr 360 365 370	1219
gct gag ctg tat cca acc att gta aga tcg ctg gct gtg gga agc ggc Ala Glu Leu Tyr Pro Thr Ile Val Arg Ser Leu Ala Val Gly Ser Gly 375 380 385	1267
agc atg gtg tgt cgc ctg gcc agc atc ctg gcg ccg ttc tct gtg gac Ser Met Val Cys Arg Leu Ala Ser Ile Leu Ala Pro Phe Ser Val Asp 390 395 400	1315
ctc agc agc att tgg atc ttc ata cca cag ttg ttt gtt ggg act atg Leu Ser Ser Ile Trp Ile Phe Ile Pro Gln Leu Phe Val Gly Thr Met 405 410 415	1363
gcc ctc ctg agt gga gtg tta aca cta aag ctt cca gaa acc ctt ggg Ala Leu Leu Ser Gly Val Leu Thr Leu Lys Leu Pro Glu Thr Leu Gly	1411

420	425	430	435	
aaa cgg cta gca act act tgg gag gag gct gca aaa ctg gag tca gag				1459
Lys Arg Leu Ala Thr Thr Trp Glu Glu Ala Ala Lys Leu Glu Ser Glu				
	440	445	450	
aat gaa agc aag tca agc aaa tta ctt ctc aca act aat aat agt ggg				1507
Asn Glu Ser Lys Ser Ser Lys Leu Leu Leu Thr Thr Asn Asn Ser Gly				
	455	460	465	
ctg gaa aaa acg gaa gcg att acc ccc agg gat tct ggt ctt ggt gaa				1555
Leu Glu Lys Thr Glu Ala Ile Thr Pro Arg Asp Ser Gly Leu Gly Glu				
	470	475	480	
taaatgtgcc atgcctgctg tctagcacct gaaatattat ttaccctaata gcctttgtat				1615
tagaggaatc ttattctcat ctcccatatg ttgtttgtat gtcttttttaa taaattttgt				1675
aagaaaattt taaagcaaat atgttataaa agaaataaaa actaagatga aaattctcag				1735
ttttaaaaaac tgctttctta ttgctgcaaa atatttttca acatttggtt ttctatgtag				1795
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aattttttgt atttttagta gggacggggg ttcaccatgt tggtcaggct ggtctcaaac	180
tacaggcgtg agccacc atg ccc gcc caa gaa gtg gaa ata tct ttt aag	230
Met Pro Ala Gln Glu Val Glu Ile Ser Phe Lys	
1 5 10	
att gga gcc tac gat cag cag ata tgg gaa aag tca atc gaa cag act	278
Ile Gly Ala Tyr Asp Gln Gln Ile Trp Glu Lys Ser Ile Glu Gln Thr	
15 20 25	
cag att aag ggt ttg aaa aac aaa ccg aaa aag atg ggc cac ata aag	326
Gln Ile Lys Gly Leu Lys Asn Lys Pro Lys Lys Met Gly His Ile Lys	
30 35 40	
cca gac ttg att gac gtt gac tta atc aga ggg tca aca ttt gcc aaa	374
Pro Asp Leu Ile Asp Val Asp Leu Ile Arg Gly Ser Thr Phe Ala Lys	
45 50 55	
gca aaa cct gaa att cca tgg aca tct ctg act cgg aag ggg ctt gtt	422
Ala Lys Pro Glu Ile Pro Trp Thr Ser Leu Thr Arg Lys Gly Leu Val	

60	65	70	75	
cga gtt gta ttt ttt cca ttg ttc agc aat tgg tgg att cag gtt acc				470
Arg Val Val Phe Phe Pro Leu Phe Ser Asn Trp Trp Ile Gln Val Thr				
	80	85	90	
tct tta aga atc ttt gtt tgg ctg tta cta ctt tat ttc atg caa gtt				518
Ser Leu Arg Ile Phe Val Trp Leu Leu Leu Leu Tyr Phe Met Gln Val				
	95	100	105	
ata gca att gtc tta tat ttg atg atg cct att gtg aac ata agt gaa				566
Ile Ala Ile Val Leu Tyr Leu Met Met Pro Ile Val Asn Ile Ser Glu				
	110	115	120	
gta ctt gga ccc ttg tgc ctt atg cta ctc atg gga act gtc cac tgt				614
Val Leu Gly Pro Leu Cys Leu Met Leu Leu Met Gly Thr Val His Cys				
	125	130	135	
caa att gtg tct act cag ata aca aga cca tca gga aac aat gga aat				662
Gln Ile Val Ser Thr Gln Ile Thr Arg Pro Ser Gly Asn Asn Gly Asn				
	140	145	150	155
cga aga aga aga aaa tta cga aaa act gta aat ggt gat ggg agc cga				710
Arg Arg Arg Arg Lys Leu Arg Lys Thr Val Asn Gly Asp Gly Ser Arg				
	160	165	170	
gaa aat gga aat aac tcc tct gat aaa gtc aga gga ata gaa act ttg				758
Glu Asn Gly Asn Asn Ser Ser Asp Lys Val Arg Gly Ile Glu Thr Leu				
	175	180	185	
gaa tct gta ccc att att ggt ggt ttt tgg gag act atc ttt ggc aac				806
Glu Ser Val Pro Ile Ile Gly Gly Phe Trp Glu Thr Ile Phe Gly Asn				
	190	195	200	
agg att aaa aga gta aaa tta ata tct aac aaa ggg act gaa act gac				854
Arg Ile Lys Arg Val Lys Leu Ile Ser Asn Lys Gly Thr Glu Thr Asp				
	205	210	215	
aat gac cca agt tgt gtc cat cct atc att aag agg aga caa tgt cga				902
Asn Asp Pro Ser Cys Val His Pro Ile Ile Lys Arg Arg Gln Cys Arg				
	220	225	230	235
cca gag att aga atg tgc caa aca aga gag aaa cca aaa ttt tca gat				950
Pro Glu Ile Arg Met Cys Gln Thr Arg Glu Lys Pro Lys Phe Ser Asp				
	240	245	250	
gga gaa aag tgc cgt agg gag gct ttt agg cgt ttg ggt aat ggg gtg				998
Gly Glu Lys Cys Arg Arg Glu Ala Phe Arg Arg Leu Gly Asn Gly Val				
	255	260	265	
tct gat gac ctg tca agt gaa gaa gat ggt gaa gca cgg aca cag atg				1046
Ser Asp Asp Leu Ser Ser Glu Glu Asp Gly Glu Ala Arg Thr Gln Met				
	270	275	280	
ata tta ttg cgt agg agt gtg gaa ggg gcc tca agt gac aat ggt tgt				1094
Ile Leu Leu Arg Arg Ser Val Glu Gly Ala Ser Ser Asp Asn Gly Cys				
	285	290	295	
gaa gtt aag aat aga aaa tca ata ctt tca agg cac cta aac tct cag				1142
Glu Val Lys Asn Arg Lys Ser Ile Leu Ser Arg His Leu Asn Ser Gln				
	300	305	310	315
gta aag aaa acc act aca agg tgg tgt cat att gtg cgg gat tca gat				1190

Val	Lys	Lys	Thr	Thr	Thr	Arg	Trp	Cys	His	Ile	Val	Arg	Asp	Ser	Asp		
				320					325					330			
agt	ctg	gct	gaa	tca	gaa	ttt	gaa	tca	gca	gcc	ttc	agc	cag	ggc	tct	1238	
Ser	Leu	Ala	Glu	Ser	Glu	Phe	Glu	Ser	Ala	Ala	Phe	Ser	Gln	Gly	Ser		
			335					340					345				
aga	tcg	ggt	gtg	agt	ggt	ggc	tct	cga	agc	ctc	aac	atg	tca	aga	aga	1286	
Arg	Ser	Gly	Val	Ser	Gly	Gly	Ser	Arg	Ser	Leu	Asn	Met	Ser	Arg	Arg		
		350					355					360					
gac	tca	gaa	agc	acc	cgc	cat	gac	tcg	gag	act	gag	gac	atg	tta	tgg	1334	
Asp	Ser	Glu	Ser	Thr	Arg	His	Asp	Ser	Glu	Thr	Glu	Asp	Met	Leu	Trp		
	365					370					375						
gac	gac	ctg	cta	cat	ggc	cca	gag	tgc	cgg	tca	tct	gtc	acc	agt	gac	1382	
Asp	Asp	Leu	Leu	His	Gly	Pro	Glu	Cys	Arg	Ser	Ser	Val	Thr	Ser	Asp		
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agt	gag	ggg	gcc	cat	gtg	aat	acc	ctt	cac	tca	ggg	acc	aaa	cgt	gac	1430	
Ser	Glu	Gly	Ala	His	Val	Asn	Thr	Leu	His	Ser	Gly	Thr	Lys	Arg	Asp		
				400					405					410			
ccc	aaa	gag	gat	gtt	ttt	cag	cag	aat	cat	tta	ttc	tgg	ctt	cag	aat	1478	
Pro	Lys	Glu	Asp	Val	Phe	Gln	Gln	Asn	His	Leu	Phe	Trp	Leu	Gln	Asn		
			415					420					425				
tca	agt	cct	tcc	tct	gat	cga	gtt	agt	gca	ata	atc	tgg	gag	ggg	aat	1526	
Ser	Ser	Pro	Ser	Ser	Asp	Arg	Val	Ser	Ala	Ile	Ile	Trp	Glu	Gly	Asn		
		430					435					440					
gag	tgc	aaa	aag	atg	gat	atg	tct	gtg	ttg	gaa	ata	agt	ggc	atc	atc	1574	
Glu	Cys	Lys	Lys	Met	Asp	Met	Ser	Val	Leu	Glu	Ile	Ser	Gly	Ile	Ile		
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Met	Ser	Arg	Val	Asn	Ala	Tyr	Gln	Gln	Gly	Val	Gly	Tyr	Gln	Met	Leu		
	460				465					470					475		
gga	aat	gtt	gtc	act	att	gga	tta	gca	ttt	ttt	cca	ttc	tta	cat	cga	1670	
Gly	Asn	Val	Val	Thr	Ile	Gly	Leu	Ala	Phe	Phe	Pro	Phe	Leu	His	Arg		
				480					485					490			
ctt	ttc	cgt	gag	aag	agc	ctt	gac	caa	cta	aag	tcc	att	tca	gct	gag	1718	
Leu	Phe	Arg	Glu	Lys	Ser	Leu	Asp	Gln	Leu	Lys	Ser	Ile	Ser	Ala	Glu		
			495					500					505				
gag	atc	ttg	act	ctc	ttt	tgt	ggg	gca	cca	cct	gtt	aca	cct	att	att	1766	
Glu	Ile	Leu	Thr	Leu	Phe	Cys	Gly	Ala	Pro	Pro	Val	Thr	Pro	Ile	Ile		
		510					515					520					
gtt	ttg	tcg	ata	att	aat	ttt	ttt	gaa	aga	ttg	tgt	ctt	act	tgg	atg	1814	
Val	Leu	Ser	Ile	Ile	Asn	Phe	Phe	Glu	Arg	Leu	Cys	Leu	Thr	Trp	Met		
		525				530					535						
ttt	ttt	ttc	atg	atg	tgt	gtg	gca	gag	aga	aca	tat	aaa	cag	aga	ttt	1862	
Phe	Phe	Phe	Met	Met	Cys	Val	Ala	Glu	Arg	Thr	Tyr	Lys	Gln	Arg	Phe		
	540				545					550					555		
tta	ttt	gca	aaa	ctc	ttc	agc	cat	att	act	tct	gcc	agg	aaa	gct	agg	1910	
Leu	Phe	Ala	Lys	Leu	Phe	Ser	His	Ile	Thr	Ser	Ala	Arg	Lys	Ala	Arg		
				560					565					570			

aaa tat gaa ata cct cat ttc aga ctt aag aag gtg gag aat att aaa Lys Tyr Glu Ile Pro His Phe Arg Leu Lys Lys Val Glu Asn Ile Lys 575 580 585	1958
ata tgg tta tca ctg cgt tcc tat cta aag aga cgg ggg cca cag cgt Ile Trp Leu Ser Leu Arg Ser Tyr Leu Lys Arg Arg Gly Pro Gln Arg 590 595 600	2006
tca gtt gat gtg gtt gta tcc tcg gtt ttc cta ctg aca ctt tcg att Ser Val Asp Val Val Val Ser Ser Val Phe Leu Leu Thr Leu Ser Ile 605 610 615	2054
gct ttc att tgt tgt gct cag gtt ctc caa gga cat aaa act ttc ctg Ala Phe Ile Cys Cys Ala Gln Val Leu Gln Gly His Lys Thr Phe Leu 620 625 630 635	2102
aat gat gct tat aac tgg gag ttt ttg atc tgg gaa aca gct tta cta Asn Asp Ala Tyr Asn Trp Glu Phe Leu Ile Trp Glu Thr Ala Leu Leu 640 645 650	2150
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tac agc aat gtt tca ata tta ctt aca gaa cag att aat tta tat ctt Tyr Ser Asn Val Ser Ile Leu Leu Thr Glu Gln Ile Asn Leu Tyr Leu 670 675 680	2246
aag atg gaa aaa aag cca aat aag aaa gaa cag ctt act cta gta aac Lys Met Glu Lys Lys Pro Asn Lys Lys Glu Gln Leu Thr Leu Val Asn 685 690 695	2294
aat gta tta aag ctg tcc acc aag ttg ttg aaa gag ctg gac aca cca Asn Val Leu Lys Leu Ser Thr Lys Leu Leu Lys Glu Leu Asp Thr Pro 700 705 710 715	2342
ttt aga ctc tat gga ctg aca atg aat ccc tta atc tac aat atc aca Phe Arg Leu Tyr Gly Leu Thr Met Asn Pro Leu Ile Tyr Asn Ile Thr 720 725 730	2390
aga gta gtt atc ctt tct gct gtc tca ggt gtt ata agt gat ctt cta Arg Val Val Ile Leu Ser Ala Val Ser Gly Val Ile Ser Asp Leu Leu 735 740 745	2438
gga ttt aat ata aga ctg tgg aaa att aaa tca taa gctg agttaaatgc Gly Phe Asn Ile Arg Leu Trp Lys Ile Lys Ser *	2488
ctggactctc cctggctgg tatcaaaact tacctatcaa ggaaagtgat gactgcagaa	2548
accagtgaga taccacactg cttgttcaca tgcacaggtg ctctcagctc tgccaaagcg	2608
aatgaatggt gtttccggag gagcaagtcc ttttccaact ggggtgtgcat gctaaaaacc	2668
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tggtaacaca aagacaattt tgtaagtgtg cgcttcagta ctgtgacagt tatgtttact	2788
ggacatagtc ttttgggcaa ctatgataga tgcccaaagc atgaagcaaa tatcttttat	2848
tggaaatatg caaattcaat acttttccat tatagtctat agaactggag atttcatttc	2908
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ggaaaaaaaa aaaa

2982

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<212> DNA
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<222> (1)..(7785)

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cag gga gat gaa agg gac atg caa cta ata gcc ctt gaa cag cta tgc      96
Gln Gly Asp Glu Arg Asp Met Gln Leu Ile Ala Leu Glu Gln Leu Cys
          20             25             30

atg ctg ctt ttg atg tct gac aac gtg gat cgt tgt ttt gaa aca tgt      144
Met Leu Leu Leu Met Ser Asp Asn Val Asp Arg Cys Phe Glu Thr Cys
          35             40             45

cct cct cgc act ttc tta cca gcc ctt tgc aaa att ttt ctt gat gaa      192
Pro Pro Arg Thr Phe Leu Pro Ala Leu Cys Lys Ile Phe Leu Asp Glu
          50             55             60

agt gct cca gac aat gta tta gag gtg aca gcc cgt gcc ata aca tac      240
Ser Ala Pro Asp Asn Val Leu Glu Val Thr Ala Arg Ala Ile Thr Tyr
          65             70             75             80

tac ctg gat gta tct gcg gaa tgt acc cga agg att gtt ggg gta gat      288
Tyr Leu Asp Val Ser Ala Glu Cys Thr Arg Arg Ile Val Gly Val Asp
          85             90             95

gga gct ata aaa gca ctt tgt aat cgt ttg gtt gta gtt gaa ctt aac      336
Gly Ala Ile Lys Ala Leu Cys Asn Arg Leu Val Val Val Glu Leu Asn
          100            105            110

aac agg act agc aga gac tta gcc gaa cag tgt gta aag gta tta gaa      384
Asn Arg Thr Ser Arg Asp Leu Ala Glu Gln Cys Val Lys Val Leu Glu
          115            120            125

ctg ata tgt act cgt gag tca gga gca gtc ttt gag gct ggt ggt ttg      432
Leu Ile Cys Thr Arg Glu Ser Gly Ala Val Phe Glu Ala Gly Gly Leu
          130            135            140

aat tgt gtg ctt acc ttc att cgt gac agt gga cat cta gtt cat aaa      480
Asn Cys Val Leu Thr Phe Ile Arg Asp Ser Gly His Leu Val His Lys
          145            150            155            160

gac acc ttg cac tct gct atg gct gtg gta tca aga ctc tgt ggc aaa      528
Asp Thr Leu His Ser Ala Met Ala Val Val Ser Arg Leu Cys Gly Lys
          165            170            175

atg gag cct caa gat tct tct tta gaa att tgt gta gaa tct ctg tct      576
Met Glu Pro Gln Asp Ser Ser Leu Glu Ile Cys Val Glu Ser Leu Ser
          180            185            190

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agt tta tta aag cat gaa gat cat cag gtt tca gat gga gct ctg cga	624
Ser Leu Leu Lys His Glu Asp His Gln Val Ser Asp Gly Ala Leu Arg	
195 200 205	
tgc ttt gca tca ctg gct gac cga ttt acc cgt cgt ggt gtt gac cca	672
Cys Phe Ala Ser Leu Ala Asp Arg Phe Thr Arg Arg Gly Val Asp Pro	
210 215 220	
gct cca tta gcc aag cat gga tta act gag gag ctg tta tct cga atg	720
Ala Pro Leu Ala Lys His Gly Leu Thr Glu Glu Leu Leu Ser Arg Met	
225 230 235 240	
gct gct gct ggt ggt act gtt tca gga cca tca tca gca tgc aaa cca	768
Ala Ala Ala Gly Gly Thr Val Ser Gly Pro Ser Ser Ala Cys Lys Pro	
245 250 255	
ggt cgc agc acc aca gga gct cca tcc acc act gca gat tcc aaa ttg	816
Gly Arg Ser Thr Thr Gly Ala Pro Ser Thr Thr Ala Asp Ser Lys Leu	
260 265 270	
agt aat cag gtg tca aca att gat ctt ctg agg tcg gag ctt cca gat	864
Ser Asn Gln Val Ser Thr Ile Asp Leu Leu Arg Ser Glu Leu Pro Asp	
275 280 285	
tca att gaa agt gca ttg cag ggt gat gaa aga tgt gtg ctt gat act	912
Ser Ile Glu Ser Ala Leu Gln Gly Asp Glu Arg Cys Val Leu Asp Thr	
290 295 300	
atg cgt ttg gtt gac ctt ctc ttg gtg cta tta ttt gaa gga cga aaa	960
Met Arg Leu Val Asp Leu Leu Val Leu Leu Phe Glu Gly Arg Lys	
305 310 315 320	
gct ttg cca aag tct agt gct gga tct aca ggc aga atc cca gga ctc	1008
Ala Leu Pro Lys Ser Ser Ala Gly Ser Thr Gly Arg Ile Pro Gly Leu	
325 330 335	
cgg aga tta gat agt tct ggg gag cgc tca cat cgg cag ctt ata gat	1056
Arg Arg Leu Asp Ser Ser Gly Glu Arg Ser His Arg Gln Leu Ile Asp	
340 345 350	
tgt att cga agt aaa gat acc gat gca ctt ata gat gca att gac aca	1104
Cys Ile Arg Ser Lys Asp Thr Asp Ala Leu Ile Asp Ala Ile Asp Thr	
355 360 365	
gga gcc ttt gaa gta aat ttt atg gat gat gta ggt cag act cta tta	1152
Gly Ala Phe Glu Val Asn Phe Met Asp Asp Val Gly Gln Thr Leu Leu	
370 375 380	
aac tgg gcc tct gct ttt gga act cag gaa atg gta gaa ttt ctt tgt	1200
Asn Trp Ala Ser Ala Phe Gly Thr Gln Glu Met Val Glu Phe Leu Cys	
385 390 395 400	
gag aga ggt gca gat gtt aat aga ggt caa agg tca tca tca tta cat	1248
Glu Arg Gly Ala Asp Val Asn Arg Gly Gln Arg Ser Ser Ser Leu His	
405 410 415	
tat gct gca tgt ttt gga aga cct caa gta gca aag act ctg tta cgg	1296
Tyr Ala Ala Cys Phe Gly Arg Pro Gln Val Ala Lys Thr Leu Leu Arg	
420 425 430	
cat ggt gca aat cca gat ctg aga gat gaa gat ggg aaa act cca tta	1344
His Gly Ala Asn Pro Asp Leu Arg Asp Glu Asp Gly Lys Thr Pro Leu	

435	440	445	
gat aaa gct cga gaa agg ggc cat agt gaa gtg gta gct att ctt cag Asp Lys Ala Arg Glu Arg Gly His Ser Glu Val Val Ala Ile Leu Gln 450 455 460			1392
tct cca ggt gat tgg atg tgt cca gtt aat aaa gga gat gat aag aaa Ser Pro Gly Asp Trp Met Cys Pro Val Asn Lys Gly Asp Asp Lys Lys 465 470 475 480			1440
aag aaa gat aca aac aaa gat gaa gaa gaa tgt aat gag ccc aaa gga Lys Lys Asp Thr Asn Lys Asp Glu Glu Glu Cys Asn Glu Pro Lys Gly 485 490 495			1488
gat ccg gaa atg gca ccc ata tac ttg aaa agg tta ttg cca gtg ttt Asp Pro Glu Met Ala Pro Ile Tyr Leu Lys Arg Leu Leu Pro Val Phe 500 505 510			1536
gca caa aca ttt cag caa act atg ctg cct tca ata agg aaa gca agt Ala Gln Thr Phe Gln Gln Thr Met Leu Pro Ser Ile Arg Lys Ala Ser 515 520 525			1584
ctt gct cta att cga aaa atg att cat ttt tgc tct gaa gca ctg tta Leu Ala Leu Ile Arg Lys Met Ile His Phe Cys Ser Glu Ala Leu Leu 530 535 540			1632
aaa gaa gtt tgt gat tct gat gtt ggt cac aat ttg cct aca ata cta Lys Glu Val Cys Asp Ser Asp Val Gly His Asn Leu Pro Thr Ile Leu 545 550 555 560			1680
gtg gaa atc act gca act gtc ctg gat caa gag gat gat gat gat ggc Val Glu Ile Thr Ala Thr Val Leu Asp Gln Glu Asp Asp Asp Asp Gly 565 570 575			1728
cac ttg ctg gct ttg cag atc ata agg gat tta gta gat aaa ggt ggt His Leu Leu Ala Leu Gln Ile Ile Arg Asp Leu Val Asp Lys Gly Gly 580 585 590			1776
gat ata ttt ttg gat cag cta gcc aga ctt ggt gta att agc aaa gtg Asp Ile Phe Leu Asp Gln Leu Ala Arg Leu Gly Val Ile Ser Lys Val 595 600 605			1824
tca acg ttg gca ggt cct tcc tct gat gat gag aat gaa gag gaa tca Ser Thr Leu Ala Gly Pro Ser Ser Asp Asp Glu Asn Glu Glu Glu Ser 610 615 620			1872
aaa cca gaa aaa gaa gat gaa cca cag gaa gat gct aaa gaa ttg caa Lys Pro Glu Lys Glu Asp Glu Pro Gln Glu Asp Ala Lys Glu Leu Gln 625 630 635 640			1920
caa ggt aaa cca tat cat tgg aga gac tgg tca atc att agg gga agg Gln Gly Lys Pro Tyr His Trp Arg Asp Trp Ser Ile Ile Arg Gly Arg 645 650 655			1968
gac tgc tta tat att tgg agt gat gca gca gcc ttg gaa tta tct aat Asp Cys Leu Tyr Ile Trp Ser Asp Ala Ala Ala Leu Glu Leu Ser Asn 660 665 670			2016
ggc agt aat gga tgg ttc aga ttt atc ttg gat gga aaa ctt gcc acc Gly Ser Asn Gly Trp Phe Arg Phe Ile Leu Asp Gly Lys Leu Ala Thr 675 680 685			2064
atg tat tca agt ggt agt ccg gaa ggt gga tct gac agt tca gaa agc			2112



Met	Tyr	Ser	Ser	Gly	Ser	Pro	Glu	Gly	Gly	Ser	Asp	Ser	Ser	Glu	Ser	
690						695					700					
cga	agt	gaa	ttc	tta	gag	aag	tta	caa	aga	gct	cga	ggc	caa	gta	aag	2160
Arg	Ser	Glu	Phe	Leu	Glu	Lys	Leu	Gln	Arg	Ala	Arg	Gly	Gln	Val	Lys	
705					710					715					720	
cca	tct	act	tca	agt	caa	cct	ata	ctg	tca	gca	cca	gga	ccc	act	aaa	2208
Pro	Ser	Thr	Ser	Ser	Gln	Pro	Ile	Leu	Ser	Ala	Pro	Gly	Pro	Thr	Lys	
					725					730					735	
ctt	act	gta	gga	aat	tgg	tca	ctg	aca	tgt	ttg	aaa	gaa	gga	gaa	att	2256
Leu	Thr	Val	Gly	Asn	Trp	Ser	Leu	Thr	Cys	Leu	Lys	Glu	Gly	Glu	Ile	
					740					745					750	
gct	att	cat	aat	tca	gat	ggc	cag	caa	gct	aca	ata	ttg	aaa	gaa	gat	2304
Ala	Ile	His	Asn	Ser	Asp	Gly	Gln	Gln	Ala	Thr	Ile	Leu	Lys	Glu	Asp	
					755										765	
tta	cct	ggc	ttt	gta	ttt	gaa	tct	aat	aga	gga	acc	aaa	cat	tca	ttt	2352
Leu	Pro	Gly	Phe	Val	Phe	Glu	Ser	Asn	Arg	Gly	Thr	Lys	His	Ser	Phe	
					770										780	
act	gca	gaa	act	tcc	ctg	ggc	tca	gaa	ttt	gtg	act	ggc	tgg	act	ggc	2400
Thr	Ala	Glu	Thr	Ser	Leu	Gly	Ser	Glu	Phe	Val	Thr	Gly	Trp	Thr	Gly	
785					790					795					800	
aaa	aga	ggc	aga	aaa	ctg	aaa	tct	aag	tta	gaa	aaa	aca	aag	caa	aag	2448
Lys	Arg	Gly	Arg	Lys	Leu	Lys	Ser	Lys	Leu	Glu	Lys	Thr	Lys	Gln	Lys	
					805										815	
gta	cga	act	atg	gct	cga	gat	tta	tac	gat	gac	cat	ttt	aaa	gct	gtt	2496
Val	Arg	Thr	Met	Ala	Arg	Asp	Leu	Tyr	Asp	Asp	His	Phe	Lys	Ala	Val	
					820										830	
gaa	agc	atg	cct	cgt	gga	gta	gtg	gta	aca	ctc	aga	aac	ata	gca	act	2544
Glu	Ser	Met	Pro	Arg	Gly	Val	Val	Val	Thr	Leu	Arg	Asn	Ile	Ala	Thr	
					835										845	
cag	tta	gag	tca	tct	tgg	gaa	ctt	cat	aca	aat	aga	caa	tgt	att	gag	2592
Gln	Leu	Glu	Ser	Ser	Trp	Glu	Leu	His	Thr	Asn	Arg	Gln	Cys	Ile	Glu	
					850										860	
agt	gag	aac	act	tgg	aga	gat	tta	atg	aag	aca	gct	tta	gaa	aac	cta	2640
Ser	Glu	Asn	Thr	Trp	Arg	Asp	Leu	Met	Lys	Thr	Ala	Leu	Glu	Asn	Leu	
865					870					875					880	
att	gta	ctt	ttg	aag	gat	gaa	aac	aca	att	tca	cca	tat	gaa	atg	tgt	2688
Ile	Val	Leu	Leu	Lys	Asp	Glu	Asn	Thr	Ile	Ser	Pro	Tyr	Glu	Met	Cys	
					885					890					895	
agc	agt	ggc	ttg	gta	caa	gca	ctt	ctt	act	gtg	tta	aac	aat	agc	atg	2736
Ser	Ser	Gly	Leu	Val	Gln	Ala	Leu	Leu	Thr	Val	Leu	Asn	Asn	Ser	Met	
					900					905					910	
gat	ttg	gat	atg	aaa	caa	gat	tgt	agt	caa	ctg	gta	gaa	aga	ata	aat	2784
Asp	Leu	Asp	Met	Lys	Gln	Asp	Cys	Ser	Gln	Leu	Val	Glu	Arg	Ile	Asn	
					915					920					925	
gtt	ttt	aaa	act	gcc	ttt	agt	gaa	aat	gaa	gat	gat	gaa	agt	cga	cca	2832
Val	Phe	Lys	Thr	Ala	Phe	Ser	Glu	Asn	Glu	Asp	Asp	Glu	Ser	Arg	Pro	
					930										940	

gca gtt gcg tta att cga aag tta ata gct gta cta gaa tct att gaa Ala Val Ala Leu Ile Arg Lys Leu Ile Ala Val Leu Glu Ser Ile Glu 945 950 955 960	2880
cgt cta cct ctc cat ttg tat gat aca cca gga tcc aca tat aac ctc Arg Leu Pro Leu His Leu Tyr Asp Thr Pro Gly Ser Thr Tyr Asn Leu 965 970 975	2928
cag ata ctt aca agg aga tta cga ttt cgg ttg gaa cgt gca cct ggt Gln Ile Leu Thr Arg Arg Leu Arg Phe Arg Leu Glu Arg Ala Pro Gly 980 985 990	2976
gaa act gca ttg att gac agg act ggc aga atg ttg aag atg gaa cct Glu Thr Ala Leu Ile Asp Arg Thr Gly Arg Met Leu Lys Met Glu Pro 995 1000 1005	3024
ttg gct aca gtt gaa tct ctg gaa cag tac ctt ttg aaa atg gta gca Leu Ala Thr Val Glu Ser Leu Glu Gln Tyr Leu Leu Lys Met Val Ala 1010 1015 1020	3072
aaa cag tgg tat gat ttt gac cga tct tca ttt gtt ttt gtt cga aaa Lys Gln Trp Tyr Asp Phe Asp Arg Ser Ser Phe Val Phe Val Arg Lys 1025 1030 1035 1040	3120
tta aga gaa gga caa aat ttt ata ttt cgg cac cag cat gat ttt gat Leu Arg Glu Gly Gln Asn Phe Ile Phe Arg His Gln His Asp Phe Asp 1045 1050 1055	3168
gaa aat gga atc att tac tgg att gga aca aat gca aaa act gct tat Glu Asn Gly Ile Ile Tyr Trp Ile Gly Thr Asn Ala Lys Thr Ala Tyr 1060 1065 1070	3216
gaa tgg gta aat cca gct gcc tat gga ctt gta gta gta acg tca tca Glu Trp Val Asn Pro Ala Ala Tyr Gly Leu Val Val Val Thr Ser Ser 1075 1080 1085	3264
gaa gga aga aat cta cct tat ggc cgc tta gaa gac ata cta agt cgt Glu Gly Arg Asn Leu Pro Tyr Gly Arg Leu Glu Asp Ile Leu Ser Arg 1090 1095 1100	3312
gat aat tca gct tta aat tgt cat agc aat gat gat aag aat gcc tgg Asp Asn Ser Ala Leu Asn Cys His Ser Asn Asp Asp Lys Asn Ala Trp 1105 1110 1115 1120	3360
ttt gcc ata gat ctg ggt ctc tgg gtg ata cca tca gca tat aca ctt Phe Ala Ile Asp Leu Gly Leu Trp Val Ile Pro Ser Ala Tyr Thr Leu 1125 1130 1135	3408
cgt cat gct cgt ggt tat gga agg tct gca ctg aga aat tgg gtt ttc Arg His Ala Arg Gly Tyr Gly Arg Ser Ala Leu Arg Asn Trp Val Phe 1140 1145 1150	3456
cag gta tcc aaa gat gga cag aac tgg act tct ttg tat acc cat gtt Gln Val Ser Lys Asp Gly Gln Asn Trp Thr Ser Leu Tyr Thr His Val 1155 1160 1165	3504
gat gac tgc agt ctc aat gaa cca ggg tca act gca act tgg cct ctt Asp Asp Cys Ser Leu Asn Glu Pro Gly Ser Thr Ala Thr Trp Pro Leu 1170 1175 1180	3552
gat cca cca aag gat gag aaa caa ggg tgg aga cat gtg aga att aaa Asp Pro Pro Lys Asp Glu Lys Gln Gly Trp Arg His Val Arg Ile Lys 1185 1190 1195 1200	3600

cag atg ggg aaa aat gcc agt gga caa aca cac tac ctc tca tta tct Gln Met Gly Lys Asn Ala Ser Gly Gln Thr His Tyr Leu Ser Leu Ser 1205 1210 1215	3648
gga ttc gaa ctt tat ggc act gta aat gga gta tgt gaa gat cag cta Gly Phe Glu Leu Tyr Gly Thr Val Asn Gly Val Cys Glu Asp Gln Leu 1220 1225 1230	3696
ggg aaa gca gct aaa gaa gca gaa gct aat ctt aga cgg cag aga cgt Gly Lys Ala Ala Lys Glu Ala Glu Ala Asn Leu Arg Arg Gln Arg Arg 1235 1240 1245	3744
cta gta cgt tcc cag gtt ctg aaa tac atg gtt cca gga gct cgt gtt Leu Val Arg Ser Gln Val Leu Lys Tyr Met Val Pro Gly Ala Arg Val 1250 1255 1260	3792
atc aga ggc ctg gat tgg aaa tgg cga gat cag gat ggc agc cca cag Ile Arg Gly Leu Asp Trp Lys Trp Arg Asp Gln Asp Gly Ser Pro Gln 1265 1270 1275 1280	3840
gga gaa ggc act gtc aca gga gaa cta cac aat ggc tgg att gat gtc Gly Glu Gly Thr Val Thr Gly Glu Leu His Asn Gly Trp Ile Asp Val 1285 1290 1295	3888
acc tgg gat gct ggt ggc tca aac tct tac cgt atg ggc gca gaa gga Thr Trp Asp Ala Gly Gly Ser Asn Ser Tyr Arg Met Gly Ala Glu Gly 1300 1305 1310	3936
aaa ttt gac ctc aag ctt gca cca ggg tac gac cct gat aca gtg gca Lys Phe Asp Leu Lys Leu Ala Pro Gly Tyr Asp Pro Asp Thr Val Ala 1315 1320 1325	3984
tca ccc aaa cct gtt tca tcc act gtt tca ggc aca acg caa tca tgg Ser Pro Lys Pro Val Ser Ser Thr Val Ser Gly Thr Thr Gln Ser Trp 1330 1335 1340	4032
agc agc ttg gtg aaa aac aac tgt cca gac aag aca tct gct gct gca Ser Ser Leu Val Lys Asn Asn Cys Pro Asp Lys Thr Ser Ala Ala Ala 1345 1350 1355 1360	4080
ggc tcc tca agt aga aaa gga agc agc agt tct gtg tgt agc gtg gcc Gly Ser Ser Ser Arg Lys Gly Ser Ser Ser Ser Val Cys Ser Val Ala 1365 1370 1375	4128
agt agc agc gac atc agc ttg ggt tcg acc aaa acg gaa cgg aga tca Ser Ser Ser Asp Ile Ser Leu Gly Ser Thr Lys Thr Glu Arg Arg Ser 1380 1385 1390	4176
gaa att gta atg gaa cac agt ata gtt tca gga gct gat gtc cat gaa Glu Ile Val Met Glu His Ser Ile Val Ser Gly Ala Asp Val His Glu 1395 1400 1405	4224
cca att gtt gtt ctt tca tct gct gaa aac gtc cct caa aca gaa gta Pro Ile Val Val Leu Ser Ser Ala Glu Asn Val Pro Gln Thr Glu Val 1410 1415 1420	4272
ggg tca tct tcc agt gca agc acc agc acc tta aca gcg gaa acg gga Gly Ser Ser Ser Ala Ser Thr Ser Thr Leu Thr Ala Glu Thr Gly 1425 1430 1435 1440	4320
agt gaa aat gct gaa agg aag tta ggc cct gat agt tct gtt cgt act Ser Glu Asn Ala Glu Arg Lys Leu Gly Pro Asp Ser Ser Val Arg Thr	4368

	1445	1450	1455	
cct ggg gag tct agt gca ata tcc atg gga att gtc agt gtt agt tct				4416
Pro Gly Glu Ser Ser Ala Ile Ser Met Gly Ile Val Ser Val Ser Ser				
	1460	1465	1470	
cct gat gtt agt tca gta tct gaa tta act aat aaa gaa gca gct tca				4464
Pro Asp Val Ser Ser Val Ser Glu Leu Thr Asn Lys Glu Ala Ala Ser				
	1475	1480	1485	
caa cga cct ctt agc tct tca gca agt aac aga ctg tca gtg agt tct				4512
Gln Arg Pro Leu Ser Ser Ser Ala Ser Asn Arg Leu Ser Val Ser Ser				
	1490	1495	1500	
ttg ttg gct gct ggg gcc cct atg agc tct agt gca agt gta cct aac				4560
Leu Leu Ala Ala Gly Ala Pro Met Ser Ser Ser Ala Ser Val Pro Asn				
1505	1510	1515	1520	
ctg tcc tca aga gaa aca tct agc ttg gag agt ttt gta agg aga gtg				4608
Leu Ser Ser Arg Glu Thr Ser Ser Leu Glu Ser Phe Val Arg Arg Val				
	1525	1530	1535	
gca aac ata gca cgg act aat gcc acg aac aac atg aat cta agc cga				4656
Ala Asn Ile Ala Arg Thr Asn Ala Thr Asn Asn Met Asn Leu Ser Arg				
	1540	1545	1550	
agc agc agt gat aac aac act aat act ttg ggg agg aat gtg atg agc				4704
Ser Ser Ser Asp Asn Asn Thr Asn Thr Leu Gly Arg Asn Val Met Ser				
	1555	1560	1565	
aca gca act tct cct ctt atg ggt gct cag agt ttc cct aat ttg acc				4752
Thr Ala Thr Ser Pro Leu Met Gly Ala Gln Ser Phe Pro Asn Leu Thr				
	1570	1575	1580	
aca cct ggt act aca tca aca gtg act atg tca aca tcc agt gtt act				4800
Thr Pro Gly Thr Thr Ser Thr Val Thr Met Ser Thr Ser Ser Val Thr				
1585	1590	1595	1600	
agc agc agc aat gta gct aca gca aca aca gtt tta tca gtt ggt caa				4848
Ser Ser Ser Asn Val Ala Thr Ala Thr Thr Val Leu Ser Val Gly Gln				
	1605	1610	1615	
tct tta agt aac act tta acc acc agc ctc aca tca act tcc agt gag				4896
Ser Leu Ser Asn Thr Leu Thr Thr Ser Leu Thr Ser Thr Ser Ser Glu				
	1620	1625	1630	
agt gac aca ggt cag gaa gca gaa tat tcc tta tat gat ttc ctt gat				4944
Ser Asp Thr Gly Gln Glu Ala Glu Tyr Ser Leu Tyr Asp Phe Leu Asp				
	1635	1640	1645	
agc tgc cgt gcc agt act cta ttg gct gag ctc gat gat gat gag gac				4992
Ser Cys Arg Ala Ser Thr Leu Leu Ala Glu Leu Asp Asp Asp Glu Asp				
	1650	1655	1660	
tta cct gag cca gat gaa gaa gat gat gag aat gaa gat gac aat cag				5040
Leu Pro Glu Pro Asp Glu Glu Asp Asp Glu Asn Glu Asp Asp Asn Gln				
1665	1670	1675	1680	
gag gac caa gaa tac gag gag gtt atg att ctg aga cgc cca tcc ctg				5088
Glu Asp Gln Glu Tyr Glu Glu Val Met Ile Leu Arg Arg Pro Ser Leu				
	1685	1690	1695	
caa cgt cga gct gcc tcc cgc tct gat gta acg cat cat gct gtt acc				5136

Gln Arg Arg Ala Gly Ser Arg Ser Asp Val Thr His His Ala Val Thr	
1700 1705 1710	
tcg cag cta cca cag gta cct gct gga gca ggg agc cga cct att ggg	5184
Ser Gln Leu Pro Gln Val Pro Ala Gly Ala Gly Ser Arg Pro Ile Gly	
1715 1720 1725	
gag cag gaa gaa gaa gag tac gaa act aaa gga gga cgc cgg aga aca	5232
Glu Gln Glu Glu Glu Glu Tyr Glu Thr Lys Gly Gly Arg Arg Arg Thr	
1730 1735 1740	
tgg gat gat gat tat gtg cta aag aga cag ttt tct gca ttg gtt cct	5280
Trp Asp Asp Asp Tyr Val Leu Lys Arg Gln Phe Ser Ala Leu Val Pro	
1745 1750 1755 1760	
gct ttt gat cct aga cct ggt cgt act aat gtc cag cag aca act gat	5328
Ala Phe Asp Pro Arg Pro Gly Arg Thr Asn Val Gln Gln Thr Thr Asp	
1765 1770 1775	
cta gaa ata cca ccc cca ggg acc cct cat tca gag ctc ttg gaa gaa	5376
Leu Glu Ile Pro Pro Pro Gly Thr Pro His Ser Glu Leu Leu Glu Glu	
1780 1785 1790	
gtc gaa tgt act ccg tca cct cga tta gct ctc act ttg aaa gta aca	5424
Val Glu Cys Thr Pro Ser Pro Arg Leu Ala Leu Thr Leu Lys Val Thr	
1795 1800 1805	
ggt ctt gga acg act cgt gaa gtt gaa tta cca ctc acc aat ttc aga	5472
Gly Leu Gly Thr Thr Arg Glu Val Glu Leu Pro Leu Thr Asn Phe Arg	
1810 1815 1820	
tca acc atc ttt tac tat gta caa aaa ttg ctt caa ttg tcc tgt aat	5520
Ser Thr Ile Phe Tyr Tyr Val Gln Lys Leu Leu Gln Leu Ser Cys Asn	
1825 1830 1835 1840	
ggc aat gtg aaa tca gat aaa ctt agg cgt att tgg gag ccc aca tac	5568
Gly Asn Val Lys Ser Asp Lys Leu Arg Arg Ile Trp Glu Pro Thr Tyr	
1845 1850 1855	
aca atc atg tac aga gaa atg aag gat tct gat aaa gaa aag gaa aat	5616
Thr Ile Met Tyr Arg Glu Met Lys Asp Ser Asp Lys Glu Lys Glu Asn	
1860 1865 1870	
gga aaa atg ggt tgc tgg tct ata gag cat gtg gag cag tac ctt ggc	5664
Gly Lys Met Gly Cys Trp Ser Ile Glu His Val Glu Gln Tyr Leu Gly	
1875 1880 1885	
act gat gaa tta cca aag aat gac ttg ata acc tac ctg cag aag aat	5712
Thr Asp Glu Leu Pro Lys Asn Asp Leu Ile Thr Tyr Leu Gln Lys Asn	
1890 1895 1900	
gca gac gct gct ttc ctg cgc cac tgg aaa tta act ggc act aat aaa	5760
Ala Asp Ala Ala Phe Leu Arg His Trp Lys Leu Thr Gly Thr Asn Lys	
1905 1910 1915 1920	
agt att agg aaa aac aga aat tgt tct cag ctc ata gct gca tat aag	5808
Ser Ile Arg Lys Asn Arg Asn Cys Ser Gln Leu Ile Ala Ala Tyr Lys	
1925 1930 1935	
gat ttt tgt gag cat gga aca aag tct ggg tta aac cag ggg gcc att	5856
Asp Phe Cys Glu His Gly Thr Lys Ser Gly Leu Asn Gln Gly Ala Ile	
1940 1945 1950	

tct act ctt caa agt agt gat att ctt aat tta aca aaa gaa caa cct Ser Thr Leu Gln Ser Ser Asp Ile Leu Asn Leu Thr Lys Glu Gln Pro 1955 1960 1965	5904
cag gcc aaa gca ggc aat gga cag aac tct tgt gga gta gaa gat gtc Gln Ala Lys Ala Gly Asn Gly Gln Asn Ser Cys Gly Val Glu Asp Val 1970 1975 1980	5952
ctt cag ctt ctg cgt att ctg tat ata gtt gca agt gac cct tat tca Leu Gln Leu Leu Arg Ile Leu Tyr Ile Val Ala Ser Asp Pro Tyr Ser 1985 1990 1995 2000	6000
aga ata tcc cag gaa gat ggt gat gaa cag cct cag ttt act ttt cca Arg Ile Ser Gln Glu Asp Gly Asp Glu Gln Pro Gln Phe Thr Phe Pro 2005 2010 2015	6048
cca gat gaa ttc act agc aaa aaa att aca aca aaa ata tta cag cag Pro Asp Glu Phe Thr Ser Lys Lys Ile Thr Thr Lys Ile Leu Gln Gln 2020 2025 2030	6096
att gag gaa cca ttg gca ctg gca agt ggg gct ctg cca gac tgg tgt Ile Glu Glu Pro Leu Ala Leu Ala Ser Gly Ala Leu Pro Asp Trp Cys 2035 2040 2045	6144
gaa caa tta acc agc aaa tgt cct ttt cta ata cca ttt gaa act aga Glu Gln Leu Thr Ser Lys Cys Pro Phe Leu Ile Pro Phe Glu Thr Arg 2050 2055 2060	6192
cag ctt tat ttc aca tgt aca gca ttt ggc gcc tca aga gca ata gta Gln Leu Tyr Phe Thr Cys Thr Ala Phe Gly Ala Ser Arg Ala Ile Val 2065 2070 2075 2080	6240
tgg tta cag aac cga cgt gaa gcc act gtg gag cga acg aga acc aca Trp Leu Gln Asn Arg Arg Glu Ala Thr Val Glu Arg Thr Arg Thr Thr 2085 2090 2095	6288
agc agt gtt agg cga gat gac cct gga gag ttt cga gtt ggt cgt ctc Ser Ser Val Arg Arg Asp Asp Pro Gly Glu Phe Arg Val Gly Arg Leu 2100 2105 2110	6336
aag cat gaa aga gta aaa gtt cca cgt ggc gag tca ctg atg gaa tgg Lys His Glu Arg Val Lys Val Pro Arg Gly Glu Ser Leu Met Glu Trp 2115 2120 2125	6384
gct gag aat gtc atg caa ata cat gca gat cgg aaa tca gtt ctt gag Ala Glu Asn Val Met Gln Ile His Ala Asp Arg Lys Ser Val Leu Glu 2130 2135 2140	6432
gtt gaa ttt tta gga gaa gaa gga act ggc ttg gga ccc aca tta gag Val Glu Phe Leu Gly Glu Glu Gly Thr Gly Leu Gly Pro Thr Leu Glu 2145 2150 2155 2160	6480
ttt tat gct ctg gtg gca gca gaa ttc cag aga act gac ttg gga gct Phe Tyr Ala Leu Val Ala Ala Glu Phe Gln Arg Thr Asp Leu Gly Ala 2165 2170 2175	6528
tgg ctt tgt gat gat aat ttt cca gat gat gaa tct cgt cac gtt gat Trp Leu Cys Asp Asp Asn Phe Pro Asp Asp Glu Ser Arg His Val Asp 2180 2185 2190	6576
ctt gga ggt gga ttg aaa cct cct gga tat tat gtg cag agg tca tgt Leu Gly Gly Gly Leu Lys Pro Pro Gly Tyr Tyr Val Gln Arg Ser Cys 2195 2200 2205	6624

gga ctg ttc aca gca cca ttt cca cag gat agt gat gag ctt gaa agg Gly Leu Phe Thr Ala Pro Phe Pro Gln Asp Ser Asp Glu Leu Glu Arg 2210 2215 2220	6672
atc acg aaa ctg ttt cat ttc ctt gga att ttc ttg gcc aaa tgc att Ile Thr Lys Leu Phe His Phe Leu Gly Ile Phe Leu Ala Lys Cys Ile 2225 2230 2235 2240	6720
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gct tct aca gaa gaa ggt cat gat tca ctc tcg gta gga agc ttt gaa Ala Ser Thr Glu Glu Gly His Asp Ser Leu Ser Val Gly Ser Phe Glu 2290 2295 2300	6912
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Ser Trp Ala Ala Glu Asp Ile Ile Asn Tyr Thr Glu Pro Lys Leu Gly			
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Cys Ser Thr Leu Pro Pro Gly Gly Leu Ala Asn Leu His Pro Arg Leu			
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Thr Val Val Arg Lys Val Asp Ala Thr Asp Ala Ser Tyr Pro Ser Val			
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Leu Asn *			
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 tcgaccacg cgtccggcg gttgtgccg atctagagag tcggggagcc gccccgcac 180  
 ccaggccttc tcgcgtgccc tggtcgtg tgaagccgc ggcgcgcgc tctcccgac 240  
 cctgcagggt aaaagaatgt cacatgtcag cttttgtacc tgaagtcagc atgcaaagtt 300  
 cagggtacat ggatgaatgc caacttttgc atttcccatg tgtatcctgt gaccattcta 360  
 tctgggaaca tccttcaaag agttcatgca tcttactgag gacacctgac cttttgaagc 420  
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 Met Ser Pro Val Phe Pro Met Leu Thr Val Leu  
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 Thr Met Phe Tyr Tyr Ile Cys Leu Arg Arg Arg Ala Arg Thr Ala Thr  
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 Arg Gly Glu Met Met Asn Thr His Arg Ala Ile Glu Ser Asn Ser Gln  
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 Thr Ser Pro Leu Asn Ala Glu Val Val Gln Tyr Ala Lys Glu Val Val  
 45 50 55  
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 Asp Phe Ser Ser His Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met  
 60 65 70 75  
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 Trp Asn Leu Ala Gly Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe  
 80 85 90  
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 Thr Gln Thr Ala Val Phe Arg Thr Tyr Gly Thr Trp Trp Asp Gln Cys  
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 Pro Ser Ala Ser Leu Pro Phe Lys Arg Thr Pro Pro Asn Phe Gln Ser  
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 cag gac tat gtg gaa ctt act ttt gaa caa cag gtg tat cct aca gct 855  
 Gln Asp Tyr Val Glu Leu Thr Phe Glu Gln Gln Val Tyr Pro Thr Ala  
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gta cat gtt cta gaa acc tat cat ccc gga gca gtc att aga att ctc	903
Val His Val Leu Glu Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu	
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Asp Pro Leu Gln Tyr Ile His Leu Asn Leu Gln Pro Tyr Trp Ala Lys	
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cta gat gac act tct ctg gaa ttt cta cag tct cgc tgc act ctt gtc	1479
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cag tgg ctt aat tta tct tgg act ggc aat aga ggc ttc atc tct gtt	1527
Gln Trp Leu Asn Leu Ser Trp Thr Gly Asn Arg Gly Phe Ile Ser Val	
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gca gga ttt agc agg ttt ctg aag gtt tgt gga tcc gaa tta gta cgc	1575
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Leu Glu Leu Ser Cys Ser His Phe Leu Asn Glu Thr Cys Leu Glu Val	

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Asp Lys Leu Pro Pro Gln Ala Phe Asn His Ile Ala Lys Leu Cys Ser				
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Leu Lys Arg Leu Val Leu Tyr Arg Thr Lys Val Glu Gln Thr Ala Leu				
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Ser Cys Val Met Ile Glu Asp Tyr Asp Val Ile Ala Ser Met Ile Gly				
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Cys Phe Thr Arg Leu Ala His Gln Leu Pro Asn Leu Gln Lys Leu Phe				
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Cys Asn Cys Thr Arg Leu Gln Gln Leu Asp Ile Leu Gly Thr Arg Met				
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Val Ser Pro Ala Ser Leu Arg Lys Leu Leu Glu Ser Cys Lys Asp Leu				
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Ser Leu Leu Asp Val Ser Phe Cys Ser Gln Ile Asp Asn Arg Ala Val				
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Thr Gln *				
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 Met Ser Pro Val Phe Pro Met Leu Thr Val Leu  
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Asp Phe Ser Ser His Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met	
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Trp Asn Leu Ala Gly Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe	
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act cag aca gct gtg ttt cga act tat ggg aca tgg tgg gat cag tgt	759
Thr Gln Thr Ala Val Phe Arg Thr Tyr Gly Thr Trp Trp Asp Gln Cys	
95 100 105	
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Val His Val Leu Glu Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu	
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ctc ctg gaa tct tgt aaa gat ctt tct tta ctt gat gtg tcc ttc tgt      2151
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tcg cag att gat aac aga gct gtg cta gaa ctg aat gca agc ttt cca      2199
Ser Gln Ile Asp Asn Arg Ala Val Leu Glu Leu Asn Ala Ser Phe Pro
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 atg gat aga atg aca gaa gat gct ctt cgc ttg aat ctg ttg aag cgg 227  
 Met Asp Arg Met Thr Glu Asp Ala Leu Arg Leu Asn Leu Leu Lys Arg  
 1 5 10 15

agc ttg gac cca gca gat gag cga gat gat gtc ctg gca aag cga ctc 275  
 Ser Leu Asp Pro Ala Asp Glu Arg Asp Asp Val Leu Ala Lys Arg Leu  
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aaa atg gag ggg cat gag gcc atg gaa cgt ctg aaa atg ttg gca ttg 323  
 Lys Met Glu Gly His Glu Ala Met Glu Arg Leu Lys Met Leu Ala Leu  
 35 40 45

ctc aaa agg aag gat ttg gca aat ctt gag gtg cca cat gag tta ccc 371  
 Leu Lys Arg Lys Asp Leu Ala Asn Leu Glu Val Pro His Glu Leu Pro  
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acc aaa cag gat ggc agt ggt gtc aag ggc tat gaa gaa aaa ctt aac 419  
 Thr Lys Gln Asp Gly Ser Gly Val Lys Gly Tyr Glu Glu Lys Leu Asn  
 65 70 75 80

ggg aat ctc agg cct cat gga gac aac agg act gct gga agg cca ggc 467  
 Gly Asn Leu Arg Pro His Gly Asp Asn Arg Thr Ala Gly Arg Pro Gly  
 85 90 95

aaa gaa aac atc aat gat gag cct gtg gat atg agt gct aga cgg agt 515  
 Lys Glu Asn Ile Asn Asp Glu Pro Val Asp Met Ser Ala Arg Arg Ser  
 100 105 110

gag cca gag cga gga agg cta act ccc tca cca gac atc att gtt ttg 563  
 Glu Pro Glu Arg Gly Arg Leu Thr Pro Ser Pro Asp Ile Ile Val Leu  
 115 120 125

tct gac aat gag gct tcc agt ccc cgt tcc agt tcc aga atg gaa gaa 611  
 Ser Asp Asn Glu Ala Ser Ser Pro Arg Ser Ser Ser Arg Met Glu Glu  
 130 135 140

aga ctc aaa gca gcc aac tta gag atg ttt aag ggg aaa ggc att gag 659  
 Arg Leu Lys Ala Ala Asn Leu Glu Met Phe Lys Gly Lys Gly Ile Glu  
 145 150 155 160

gag cgg cag cag ctt atc aag cag ctg agg gat gag cta cga ttg gaa 707  
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 165 170 175

gaa gcc cga ctg gtc ctg tta aag aaa ctg aga cag agt cag cta cag 755  
 Glu Ala Arg Leu Val Leu Leu Lys Lys Leu Arg Gln Ser Gln Leu Gln  
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aaa gag aat gtg gtc cag aag act cca gtt gta cag aat gca gca tct 803  
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 195 200 205

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 Ile Val Gln Pro Ser Pro Ala His Val Gly Gln Gln Gly Leu Ser Lys  
 210 215 220

ctt ccc tct cgg cct ggg gcc caa ggg gtt gaa cct caa aat ttg aga 899  
 Leu Pro Ser Arg Pro Gly Ala Gln Gly Val Glu Pro Gln Asn Leu Arg  
 225 230 235 240

aca tta cag ggt cac agt gtc atc cgt tca gct acc aat acc acc ctt	947
Thr Leu Gln Gly His Ser Val Ile Arg Ser Ala Thr Asn Thr Thr Leu	
245 250 255	
cca cac atg ttg atg tct caa cgt gtt att gca cca aac cca gcc cag	995
Pro His Met Leu Met Ser Gln Arg Val Ile Ala Pro Asn Pro Ala Gln	
260 265 270	
cta cag ggt cag cgg ggc ccg cct aag cct ggc ctt gta cgc acc aca	1043
Leu Gln Gly Gln Arg Gly Pro Pro Lys Pro Gly Leu Val Arg Thr Thr	
275 280 285	
aca ccc aac atg aat ccc gcc atc aat tat caa ccg cag tca agt tct	1091
Thr Pro Asn Met Asn Pro Ala Ile Asn Tyr Gln Pro Gln Ser Ser Ser	
290 295 300	
tct gtt cca tgt cag cgt aca aca tcc tct gcc atc tat atg aac ctt	1139
Ser Val Pro Cys Gln Arg Thr Thr Ser Ser Ala Ile Tyr Met Asn Leu	
305 310 315 320	
gct tct cat atc cag cca ggg acg gtg aac aga gtg tcc tcg cca ctt	1187
Ala Ser His Ile Gln Pro Gly Thr Val Asn Arg Val Ser Ser Pro Leu	
325 330 335	
cct agc ccc agc gcc atg act gat gct gcc aac tca cag gct gca gcc	1235
Pro Ser Pro Ser Ala Met Thr Asp Ala Ala Asn Ser Gln Ala Ala Ala	
340 345 350	
aaa ttg gct ctt cgc aaa cag ctg gaa aag aca ctc ctg gag atc cca	1283
Lys Leu Ala Leu Arg Lys Gln Leu Glu Lys Thr Leu Leu Glu Ile Pro	
355 360 365	
ccc cct aaa cct cct gct ccc tta ctt cat ttc ttg cct agt gca gcc	1331
Pro Pro Lys Pro Pro Ala Pro Leu Leu His Phe Leu Pro Ser Ala Ala	
370 375 380	
aat agc gag ttc atc tac atg gta ggc ttg gaa gaa gtc gta cag agt	1379
Asn Ser Glu Phe Ile Tyr Met Val Gly Leu Glu Glu Val Val Gln Ser	
385 390 395 400	
gtc att gac agc caa ggc aaa agc tgt gcc tca ctt ctg cgg gtt gaa	1427
Val Ile Asp Ser Gln Gly Lys Ser Cys Ala Ser Leu Leu Arg Val Glu	
405 410 415	
ccc ttt gta tgt gcc cag tgc cgc aca gat ttc acc cct cac tgg aag	1475
Pro Phe Val Cys Ala Gln Cys Arg Thr Asp Phe Thr Pro His Trp Lys	
420 425 430	
caa gaa aag aat ggt aag att cta tgt gag cag tgt atg acc tcc aac	1523
Gln Glu Lys Asn Gly Lys Ile Leu Cys Glu Gln Cys Met Thr Ser Asn	
435 440 445	
cag aaa aag gct cta aaa gct gaa cac acc aac cgg ctg aaa aat gca	1571
Gln Lys Lys Ala Leu Lys Ala Glu His Thr Asn Arg Leu Lys Asn Ala	
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Phe Val Lys Ala Leu Gln Gln Glu Gln Val Arg Ile Leu Thr Ala His	
465 470 475 480	
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Trp Pro Pro Val Pro Val Cys Phe Phe Gln Arg Val Ala Pro Ser Ser	
485 490 495	

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 Leu Gln Glu Trp Phe Met \*  
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 acgaaagaaa gagtgaatta tgaagtagcc cagtgaagag tagtggttct agagtatgtg 2020  
 aacatctcat gtagcagta taggatgaga atatcttaga gaaggaaaaa tgtgttggga 2080  
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 aggtcagaat cgctacctat tgtccaaagc agtcgtaaga agaggtccca atccccact 180  
 ctttccgccc taatggaggt ctccagtttc ggtaaaagtt tcatttgatc tgaatagtat 240  
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 caaggctccc ttgccagcag ggtgctgcca ataaaaggta gtcacgtgga atttgga 357  
 atg tgg aaa gga ggt aga agt cat cct ttc ctc ccc tgt agc agc agg 405  
 Met Trp Lys Gly Gly Arg Ser His Pro Phe Leu Pro Cys Ser Ser Arg  
 1 5 10 15  
 cgt gca ggc tct ggt ggt cag ctg gac tcc ata ctc ccc cac cag tca 453  
 Arg Ala Gly Ser Gly Gly Gln Leu Asp Ser Ile Leu Pro His Gln Ser  
 20 25 30  
 cca gcc tgg gga ccg tgg ggc tgc aag gac ctc agc agc ggt gtc cca 501  
 Pro Ala Trp Gly Pro Trp Gly Cys Lys Asp Leu Ser Ser Gly Val Pro  
 35 40 45  
 agt ttc ctg act tct tcc atc ctc tgg aaa tca gct gtg ttt gct gag 549  
 Ser Phe Leu Thr Ser Ser Ile Leu Trp Lys Ser Ala Val Phe Ala Glu  
 50 55 60

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gat aat ggc ctc aag atc cat ccg tgt tcc tgc aaa aga cat gat ctc      597
Asp Asn Gly Leu Lys Ile His Pro Cys Ser Cys Lys Arg His Asp Leu
 65              70              75              80

gct gtt ttt tat ggt tgc aca tct ttt gtt cta acg ttt ggt ctt tca      645
Ala Val Phe Tyr Gly Cys Thr Ser Phe Val Leu Thr Phe Gly Leu Ser
      85              90              95

ccc tgg ttc ctg aca cag agc ttc cta aat ccc ttg gaa ttt tct ggg      693
Pro Trp Phe Leu Thr Gln Ser Phe Leu Asn Pro Leu Glu Phe Ser Gly
      100             105             110

tgataggagt gtcctttggt ctcatgaggt gactcttggt gggctcctta tttggagact      753

ggtcatacaaa aaacctcact atgggtggaa gcgttgtgct gtcagcccca ttcccatcc      813

tctggggtag gaaatggagc tggagctcaa tcatacctac gtgataaagc ctccagaaaa      873

ctccttgaaa gacaggactt ggagagcttc cgggttggcg aacacatcca tgttccagga      933

gagtgggtgca cccaactcc acaaggaccc ttccaaacct caccctgtgt atctcttcaa      993

ctggcttcat catttgtgtc ctttaaaata tcctttgtaa taaatcagca ctagtaagaa     1053

aactgttttc ctgggttcca tgagctgttc tagcaaatgt tcaaacctga ggagggagtt     1113

gtggggacct ccaatttaca gccagttggt cagatgcata ggtgatgctt ggccttgac      1173

ctggggtctg acatgaggat ggtcctgtgt gactgagccc ttaacctgtg gagtctggtg     1233

ctcactctgc ttagggcttc tcttgccctt ttagtgcctt tctaggcggc cggacgcgtg     1293

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<220>  
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ctcaggctcc tctcctcgc tctccgccgc ctccgccgga ctccgcagg ccctgcaccg     180

ccgccgccag gctagcggag ctgccccggg aagctgggtg acgggttcgc ggctgccgcc     240

ggactgcggc ctactccgcc gcctctcagt gctattgtcc ctgggcctgg ccttgagcgg     300

gtccactggg gaaggccgtg tgcgcgggct ccgcggaag   atg ccg gac caa gcc      354
              Met Pro Asp Gln Ala
              1              5

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cta cag cag atg ctg gac aga agt tgc tgg gtt tgt ttt gct act gat	402
Leu Gln Gln Met Leu Asp Arg Ser Cys Trp Val Cys Phe Ala Thr Asp	
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gaa gat gat aga aca gct gaa tgg gtg aga cca tgc agg tgc aga gga	450
Glu Asp Asp Arg Thr Ala Glu Trp Val Arg Pro Cys Arg Cys Arg Gly	
25 30 35	
tct aca aaa tgg gtt cac cag gcc tgt cta caa cgc tgg gtg gat gaa	498
Ser Thr Lys Trp Val His Gln Ala Cys Leu Gln Arg Trp Val Asp Glu	
40 45 50	
aag caa aga gga aac agt aca gcc aga gtg gca tgt cct cag tgc aat	546
Lys Gln Arg Gly Asn Ser Thr Ala Arg Val Ala Cys Pro Gln Cys Asn	
55 60 65	
gct gaa tac cta ata gtt ttt cca aaa ttg ggt cca gtg gtt tac gtc	594
Ala Glu Tyr Leu Ile Val Phe Pro Lys Leu Gly Pro Val Val Tyr Val	
70 75 80 85	
ttg gat ctt gca gat aga ctg atc tca aaa gcc tgt cca ttt gct gca	642
Leu Asp Leu Ala Asp Arg Leu Ile Ser Lys Ala Cys Pro Phe Ala Ala	
90 95 100	
gca gga ata atg gtc ggc tct atc tat tgg aca gct gtg act tat gga	690
Ala Gly Ile Met Val Gly Ser Ile Tyr Trp Thr Ala Val Thr Tyr Gly	
105 110 115	
gca gtg aca gtg atg cag gtt gta ggt cat aaa gaa ggt ctg gat gtt	738
Ala Val Thr Val Met Gln Val Val Gly His Lys Glu Gly Leu Asp Val	
120 125 130	
atg gag aga gct gat cct tta ttc ctt tta att gga ctt cct act att	786
Met Glu Arg Ala Asp Pro Leu Phe Leu Leu Ile Gly Leu Pro Thr Ile	
135 140 145	
cct gtc atg ctg ata tta ggc aag atg att cgc tgg gag gac tat gtg	834
Pro Val Met Leu Ile Leu Gly Lys Met Ile Arg Trp Glu Asp Tyr Val	
150 155 160 165	
ctt aga ctg tgg cgc aaa tac tcg aat aaa cta caa att tta aat agt	882
Leu Arg Leu Trp Arg Lys Tyr Ser Asn Lys Leu Gln Ile Leu Asn Ser	
170 175 180	
ata ttt cca ggg ata ggt tgt cct gtt cct cga att cca gct gag gcc	930
Ile Phe Pro Gly Ile Gly Cys Pro Val Pro Arg Ile Pro Ala Glu Ala	
185 190 195	
aat cct tta gca gat cat gtc tct gct act cga atc ttg tgt gga gcc	978
Asn Pro Leu Ala Asp His Val Ser Ala Thr Arg Ile Leu Cys Gly Ala	
200 205 210	
ctt gtc ttt cct act att gct aca ata gtt ggt aaa ttg atg ttc agt	1026
Leu Val Phe Pro Thr Ile Ala Thr Ile Val Gly Lys Leu Met Phe Ser	
215 220 225	
agt gtt aac tct aat tta caa agg aca atc ttg ggt gga att gcg ttt	1074
Ser Val Asn Ser Asn Leu Gln Arg Thr Ile Leu Gly Gly Ile Ala Phe	
230 235 240 245	
gtt gcc ata aaa gga gca ttt aaa gtt tac ttc aaa cag cag caa tat	1122
Val Ala Ile Lys Gly Ala Phe Lys Val Tyr Phe Lys Gln Gln Gln Tyr	

	250	255	260	
tta cga cag gca cac cgc aaa att ctg aat tat cca gaa caa gaa gaa				1170
Leu Arg Gln Ala His Arg Lys Ile Leu Asn Tyr Pro Glu Gln Glu Glu				
	265	270	275	
gca taa aactgacttc tgggtttgtt ctgcagttct ctcatacctta tgatctgttg				1226
Ala *				
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tatttttaag aaatataata aagcacttag ggcaggggag atcatctcgg taatcatgga				1346
acctaaggat gtgatttggt ttcattgttt gtatgtacta cttttatggc agtcatatga				1406
accattatct tagcatggta aacctgggtt ttgttcatat tttctccaga cagaaatgca				1466
aagatcaaac tgtgcaaata ttaaaaaaat gcacatgctg ttttattcaa atgcctcttt				1526
tgtacatggt catgttttagt gttttctcag aatcagcaac tcaaggtaact atgaggattt				1586
ttctcactga cataatttga ttacatacta aataagagga tatgttaata tgaggaaatg				1646
taaattaaat tagttataaa taaataacca aaaatgtatg taaacattca aatgattatc				1706
tgaacaaatg agattttgtg gtgttttctt taacctatgt gatgtcctcc aaaatgtgta				1766
gggtaaaaat tcacaggggt tccagatcac tttttcaata ttaaatttta tttacataaa				1826
aaaaaaaaa aaaaaagggc ggccgctcta gagtatccct cgagggggccc aagcttacgc				1886
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aca gct ggt tat aag acc ctt ctc aag tgc ctc tca ggt aaa ttc tgc	96
Thr Ala Gly Tyr Lys Thr Leu Leu Lys Cys Leu Ser Gly Lys Phe Cys	
20 25 30	
cgc cgg gag ctg att ggc atc atg ggc ccc tca ggg gct ggc aag tct	144
Arg Arg Glu Leu Ile Gly Ile Met Gly Pro Ser Gly Ala Gly Lys Ser	
35 40 45	
aca ttc atg aac atc ttg gca gga tac agg gag tct gga atg aag ggg	192
Thr Phe Met Asn Ile Leu Ala Gly Tyr Arg Glu Ser Gly Met Lys Gly	
50 55 60	

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gtg ttg gaa gcc atg atg gtc tct gct aac ctg aag ctg agt gag aag Val Leu Glu Ala Met Met Val Ser Ala Asn Leu Lys Leu Ser Glu Lys 100 105 110	336
cag gag gtg aag aag gag ctg gtg aca gag atc ctg acg gca ctg ggc Gln Glu Val Lys Lys Glu Leu Val Thr Glu Ile Leu Thr Ala Leu Gly 115 120 125	384
ctg atg tgc tgc tcc cac acg agg aca gcc ctg ctc tct ggc ggg cag Leu Met Ser Cys Ser His Thr Arg Thr Ala Leu Leu Ser Gly Gly Gln 130 135 140	432
agg aag cgt ctg gcc atc gcc ctg gag ctg gtc aac aac ccg cct gtc Arg Lys Arg Leu Ala Ile Ala Leu Glu Leu Val Asn Asn Pro Pro Val 145 150 155 160	480
atg ttc ttt gat gag ccc acc agt ggt ctg gat agc gcc tct tgt ttc Met Phe Phe Asp Glu Pro Thr Ser Gly Leu Asp Ser Ala Ser Cys Phe 165 170 175	528
caa gtg gtg tcc ctc atg aag tcc ctg gca cag ggg ggc cgt acc atc Gln Val Val Ser Leu Met Lys Ser Leu Ala Gln Gly Gly Arg Thr Ile 180 185 190	576
atc tgc acc atc cac cag ccc agt gcc aag ctc ttt gag atg ttt gac Ile Cys Thr Ile His Gln Pro Ser Ala Lys Leu Phe Glu Met Phe Asp 195 200 205	624
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gga ctc ggc ttg cat tgc ccc acc tac cac aac ccg gct gac ttc atc Gly Leu Gly Leu His Cys Pro Thr Tyr His Asn Pro Ala Asp Phe Ile 225 230 235 240	720
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cct gtc ctc ttg ttc tcc ggc ttc ttt gtc agc ttc aag acc atc ccc Pro Val Leu Leu Phe Ser Gly Phe Phe Val Ser Phe Lys Thr Ile Pro 385 390 395 400	1200
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Tyr Glu Ala Val Gly Lys Asp Asn Pro Val Val Leu Cys Gly Trp Lys			
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Gly Cys Thr Cys Thr Phe Lys Asp Arg Ser Lys Leu Arg Glu His Leu			
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Arg Ser His Thr Gln Glu Lys Val Val Ala Cys Pro Thr Cys Gly Gly			
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tca ttg gat cag cag cac ttc cag tgt tct cac tgt tcc aag aga ttt			1968
Ser Leu Asp Gln Gln His Phe Gln Cys Ser His Cys Ser Lys Arg Phe			
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Tyr Lys Cys Pro Leu Cys Asp Met Thr Cys Pro Leu Pro Ser Ser Leu			
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Arg Asn His Met Arg Phe Arg His Ser Glu Asp Arg Pro Phe Lys Cys			
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Asp Cys Cys Asp Tyr Ser Cys Lys Asn Leu Ile Asp Leu Gln Lys His			
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Leu Asp Thr His Ser Glu Glu Pro Ala Tyr Arg Cys Asp Phe Glu Asn			
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Cys Thr Phe Ser Ala Arg Ser Leu Cys Ser Ile Lys Ser His Tyr Arg			
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Leu	Gly	Thr	Ser	Leu	Asn	Glu	Ser	Ser	Leu	Gln	Gly	Ile	Ile	Leu	Glu		
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Thr	Val	Pro	Gly	Glu	Pro	Gly	Arg	Lys	Glu	Glu	Glu	Glu	Glu	Gly	Lys		
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Gly	Ser	Glu	Gly	Thr	Ala	Leu	Ser	Ala	Ser	Gln	Asp	Asn	Pro	Ser	Ser		
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gtc	atc	cac	gtg	gtg	aat	cag	acc	aat	gcc	caa	ggc	cag	caa	gag	att		2688
Val	Ile	His	Val	Val	Asn	Gln	Thr	Asn	Ala	Gln	Gly	Gln	Gln	Glu	Ile		
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gtc	tac	tat	gtg	ctg	tct	gaa	gcc	cca	ggg	gag	cct	ccc	cca	gtc	cct		2736
Val	Tyr	Tyr	Val	Leu	Ser	Glu	Ala	Pro	Gly	Glu	Pro	Pro	Pro	Val	Pro		
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Glu	Pro	Pro	Ser	Gly	Gly	Ile	Met	Glu	Lys	Leu	Gln	Gly	Ile	Ala	Glu		
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gag	cca	gag	atc	cag	atg	gtt	tga	aggccgcaga	gccagaccat	ttcttcccca							2838
Glu	Pro	Glu	Ile	Gln	Met	Val	*										
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Val Tyr Pro Ser Tyr Pro Asp Leu Val Ile Asp Val Gly Glu Val Thr
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Leu Gly Glu Glu Asn Arg Lys Lys Leu Gln Lys Thr Gln Arg Asp Gln
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Glu Arg Ala Arg Val Ile Arg Ala Ala Cys Ala Leu Leu Asn Ser Gly
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Gly Gly Val Ile Gln Met Glu Met Ala Asn Arg Asp Glu Arg Pro Thr
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Glu Met Gly Leu Asp Leu Glu Glu Ser Leu Arg Lys Leu Ile Gln Tyr
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cca tat ttg cag gct ttc ttt gag act aag caa cac gga agg tgt ttt      518
Pro Tyr Leu Gln Ala Phe Phe Glu Thr Lys Gln His Gly Arg Cys Phe
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Tyr Ile Phe Val Lys Ser Trp Ser Gly Asp Pro Phe Leu Lys Asp Gly
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Ser Phe Asn Ser Arg Ile Cys Ser Leu Thr Ser Ala Ile Tyr Met Gln
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Ser Ile Leu Asn Glu Arg Val Glu Leu Leu Gln Arg Gln Trp Glu Glu  
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 1 5  
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 Ser Leu Leu Lys Asp Thr Leu Ser Ala Tyr Ile Ser Ala Asp Asp Ile  
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PCT/US00/34960

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Gln Leu Lys Ala Phe Gln Gln Glu Ile Ser Leu Asn His Asn Lys Ile	
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Gly Tyr Met Lys Leu Leu Gly Glu Cys Ser Ser Ile Asp Ser Val	
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Lys Leu Lys Glu Leu Gln Lys Ala Val Asp His Arg Lys Ala Ile Ile	
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925 930 935	

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aggcagctag gcgtggctct cattccttcc cacaga atg gat tat aag tcg agc 174
Met Asp Tyr Lys Ser Ser
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Leu Ile Gln Asp Gly Asn Pro Met Glu Asn Leu Glu Lys Gln Leu Ile
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Cys Pro Ile Cys Leu Glu Met Phe Thr Lys Pro Val Val Ile Leu Pro
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Cys Gln His Asn Leu Cys Arg Lys Cys Ala Asn Asp Ile Phe Gln Ala
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Gly Arg Phe Arg Cys Pro Thr Cys Arg His Glu Val Ile Met Asp Arg
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cac ccc atg tgc aag gag cac gaa gat gag aaa atc aac atc tac tgt			558
His Pro Met Cys Lys Glu His Glu Asp Glu Lys Ile Asn Ile Tyr Cys			
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Lys Val Gln Val Met Leu Pro His *			
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att cag aga ctc atg tca cat gaa gtc gtg tct gag act gca gct gga      759
Ile Gln Arg Leu Met Ser His Glu Val Val Ser Glu Thr Ala Ala Gly
   90                               95                               100                               105

aat ata att aac atg ctt tgg cag cta atg gag aat agt ctt gaa gaa      807
Asn Ile Ile Asn Met Leu Trp Gln Leu Met Glu Asn Ser Leu Glu Glu
   110                               115                               120

ctt aag cta ctt caa aca gtt ctt gtt ctt tta aca acc aat aca gta      855
Leu Lys Leu Leu Gln Thr Val Leu Val Leu Thr Thr Asn Thr Val
   125                               130                               135

gtt cat gat gag gca ctt tct aag gta gga aaa ctg ttt gcc aga gtt      903
Val His Asp Glu Ala Leu Ser Lys Val Gly Lys Leu Phe Ala Arg Val
   140                               145                               150

cat atg tgc ttt gag aca gta ttt gaa taa g ctggctgaaa gagaaaagct      954

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His Met Cys Phe Glu Thr Val Phe Glu \*  
 155 160

tgggtgccatt tgaacacaaa gcaacttccc tacagctatg gtgatgattg acattgcatg 1014  
 ttaataactg ttggtacctt atttttttcca ggtagaggtt gaaatcacgt tgggggtgctt 1074  
 aagcaaagcc ccttgggtac agcaacaggc tgagtgtga ataggaaatg gaaaaaagag 1134  
 agaaagtagc ccaagagtaa gaataggga ggaggggaact aaaaaaaaaa aa 1186

<210> 476  
 <211> 1710  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (514) .. (1263)

<400> 476  
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 tgccgcgcgc tgccgctttg ccgctgcagc catcctctt actccttgcc ttctgtcccc 120  
 gtcgtctcct ctgccgcgct gccgcagccg caccagcatc gacaacagct aagtggccga 180  
 ttccggggact tgggggtcggg gttggggcgg acgcaaggca cgaacagcac tcgcgagccc 240  
 gccatctcta cgtcagccgc cactgctgca gtaacccttc tagggcgaga gaggaaagca 300  
 ctgtggagag gcacacgctg tcccagtgt caccggttaga gtccgagcgt ttctgccaaa 360  
 accttggtga gagccttgca cttggagaag ggagcacaga ccaggtcttt gagatcgcaa 420  
 aaaatatata tatcatattg catagtgttg actttttgtc agtttaatcg accagggcag 480  
 cagctttccc caagccctct taatccctga gct atg tct cct cca acc gtg cct 534  
 Met Ser Pro Pro Thr Val Pro  
 1 5  
 ccg atg ggg gta gat ggc gtg tcc gca tac ctg atg aag aaa agg cac 582  
 Pro Met Gly Val Asp Gly Val Ser Ala Tyr Leu Met Lys Lys Arg His  
 10 15 20  
 acc cac agg aag caa cgg cgc aag ccc act ttc ctc act cgt agg aac 630  
 Thr His Arg Lys Gln Arg Arg Lys Pro Thr Phe Leu Thr Arg Arg Asn  
 25 30 35  
 atc gtg ggc tgc cgc att caa cac ggc tgg aag gaa ggc aac gag cca 678  
 Ile Val Gly Cys Arg Ile Gln His Gly Trp Lys Glu Gly Asn Glu Pro  
 40 45 50 55  
 gtg gag cag tgg aag ggt act gtg ctc gag cag gtt tcc gtg aag ccc 726  
 Val Glu Gln Trp Lys Gly Thr Val Leu Glu Gln Val Ser Val Lys Pro  
 60 65 70  
 act ctt tac atc att aaa tat gat ggc aaa gat agt gtg tat gga cta 774  
 Thr Leu Tyr Ile Ile Lys Tyr Asp Gly Lys Asp Ser Val Tyr Gly Leu  
 75 80 85

gaa ctg cac cgc gat aag aga gtt tta gcg cta gag atc ctt cct gag 822  
 Glu Leu His Arg Asp Lys Arg Val Leu Ala Leu Glu Ile Leu Pro Glu  
 90 95 100

aga gtg cca act cct cgt atc gat tca cga ctg gca gat tcc ctg att 870  
 Arg Val Pro Thr Pro Arg Ile Asp Ser Arg Leu Ala Asp Ser Leu Ile  
 105 110 115

ggc aag gca gtg gag cat gtg ttt gaa ggt gaa cat ggt acc aag gat 918  
 Gly Lys Ala Val Glu His Val Phe Glu Gly Glu His Gly Thr Lys Asp  
 120 125 130 135

gaa tgg aag ggt atg gtc ctg gcg cga gct cct gtg atg gat act tgg 966  
 Glu Trp Lys Gly Met Val Leu Ala Arg Ala Pro Val Met Asp Thr Trp  
 140 145 150

ttt tac atc acc tac gag aaa gat cct gtt ctc tat atg tac acg ctg 1014  
 Phe Tyr Ile Thr Tyr Glu Lys Asp Pro Val Leu Tyr Met Tyr Thr Leu  
 155 160 165

ctt gat gac tac aaa gat ggt gac tta cgc att att cca gat tcc aac 1062  
 Leu Asp Asp Tyr Lys Asp Gly Asp Leu Arg Ile Ile Pro Asp Ser Asn  
 170 175 180

tac tat ttc cct aca gca gaa cag gag cct gga gag gtg gtc gac agt 1110  
 Tyr Tyr Phe Pro Thr Ala Glu Gln Glu Pro Gly Glu Val Val Asp Ser  
 185 190 195

ctc gtg ggc aag cag gtg gag cat gcc aaa gat gac ggg tcc aag aga 1158  
 Leu Val Gly Lys Gln Val Glu His Ala Lys Asp Asp Gly Ser Lys Arg  
 200 205 210 215

act ggc att ttt ata cat caa gtg gtg gcg aag cct tct gtt tac ttc 1206  
 Thr Gly Ile Phe Ile His Gln Val Val Ala Lys Pro Ser Val Tyr Phe  
 220 225 230

att aag ttt gat gat gat att cac att tat gtc tat ggt tgg gtg aaa 1254  
 Ile Lys Phe Asp Asp Asp Ile His Ile Tyr Val Tyr Gly Trp Val Lys  
 235 240 245

act cct taa attcttt gtgctcttta gagaagttgt ggatctgtta gatgtgaata 1310  
 Thr Pro \*  
 250

attttgtgta ctgtagttg tgaacgccga gaagagttta ggtgtcagaa attcaggaaa 1370

gtggataaat cttatggtgc caacaaatct taccttgact aagtccacaa atttgcctca 1430

agtgtacttt gctacttttg atattgcctt gttctgtaac ttaacagtta aattgggtgc 1490

taatagaaaa ttaaaaagtg tttgcaacca ttggaacaat gcaaaaaatag attaagaaaa 1550

attaatggtg taaaccacac ccccgctcct accccttcct ttccttacct tgtttcttcc 1610

cagaaaacaa gtgttgagga tgccaagtac atccttccac ctattttccc catcttcacg 1670

cagaaagtat gttctagtag tttctgtaaa aatggcaagc 1710

<211> 2131  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (104)..(733)

<400> 477  
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 atgacatgag attgttcttt atttttcttc agctgggtttt ccc atg ggc tat gca 115  
 Met Gly Tyr Ala  
 1  
 gca gca gct cct gcc tat tct cct aac atg tat cct gga gcg aat cct 163  
 Ala Ala Ala Pro Ala Tyr Ser Pro Asn Met Tyr Pro Gly Ala Asn Pro  
 5 10 15 20  
 acc ttc caa aca ggt tac act cct ggc aca cct tac aaa gtg tcc tgt 211  
 Thr Phe Gln Thr Gly Tyr Thr Pro Gly Thr Pro Tyr Lys Val Ser Cys  
 25 30 35  
 tcc ccc acc agc ggg gct gtg cca ccg tac tcc tcc tcc ccg aac ccc 259  
 Ser Pro Thr Ser Gly Ala Val Pro Tyr Ser Ser Ser Pro Asn Pro  
 40 45 50  
 tac cag act gcc gtg tac cct gtg cga agt gcc tac ccc cag cag agc 307  
 Tyr Gln Thr Ala Val Tyr Pro Val Arg Ser Ala Tyr Pro Gln Gln Ser  
 55 60 65  
 ccg tat gca cag caa ggc acg tac tac aca cag ccg ctg tat gca gca 355  
 Pro Tyr Ala Gln Gln Gly Thr Tyr Tyr Thr Gln Pro Leu Tyr Ala Ala  
 70 75 80  
 cct cct cac gtc atc cac cac acc acg gtg gtg cag ccc aac ggc atg 403  
 Pro Pro His Val Ile His His Thr Thr Val Val Gln Pro Asn Gly Met  
 85 90 95 100  
 cct gca acg gtg tac cct gct ccc atc ccc cct cct aga ggc aac ggg 451  
 Pro Ala Thr Val Tyr Pro Ala Pro Ile Pro Pro Pro Arg Gly Asn Gly  
 105 110 115  
 gtc acc atg ggc atg gtg gct ggg acc agc cat ggc cat gtc agc agg 499  
 Val Thr Met Gly Met Val Ala Gly Thr Ser His Gly His Val Ser Arg  
 120 125 130  
 tac cct gct gac tgc tca ctc ccc aac tcc tgt cgc ccc cca ccc ggt 547  
 Tyr Pro Ala Asp Cys Ser Leu Pro Asn Ser Cys Arg Pro Pro Pro Gly  
 135 140 145  
 cac tgt gcc cac gta ccg ggc ccc agg aac gcc cac tta cag cta tgt 595  
 His Cys Ala His Val Pro Gly Pro Arg Asn Ala His Leu Gln Leu Cys  
 150 155 160  
 gcc ccc tca gtg gtg atc acc tgc aaa tgt ttg agg acg gag ctg tgc 643  
 Ala Pro Ser Val Val Ile Thr Cys Lys Cys Leu Arg Thr Glu Leu Cys  
 165 170 175 180  
 agt cac att att ggg gat tcc aca gct ggt gct gca ggc ctt gcg cct 691  
 Ser His Ile Ile Gly Asp Ser Thr Ala Gly Ala Ala Gly Leu Ala Pro  
 185 190 195

WO 01/53453

PCT/US00/34960

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cca acc agg act ttc ttc tta atg ctc tcg aca ctt agc taa acacgac      740
Pro Thr Arg Thr Phe Phe Leu Met Leu Ser Thr Leu Ser  *
                200                205                210

tatatcccgg cccagcaggc cccagcgccg ttagtctcca gctgactctg tgggttggtc      800
ttaaagcaaa ttctgttttg tggactgcct ggcaattttt tagctaactg taatgataaa      860
aaggaggatg taatctattc tgaatcacag aacattaaac agtacaataa tccattgctt      920
cataggttca agttacataa attaaagtca aataattgga aactgattca atagggaaaa      980
ctatacatga aatgaaggtc aaaaggagct atacagcaat atttcattgt ttatagatta     1040
tgagttactt tcaggacctt aacaaagatt ctgaatattt agacttcctt tgttgatttt     1100
tataacttaa tatctcccta cctatactga gtcaaaactac ttgacaaaaa catctgattt     1160
aggaaagcat ctagctttat agcacaagtt tttccatcta cagttactat cttcaaagga     1220
atatacatca caatgttgac aaaaaaacct cctgggtcct tttgaacaat gtgcaataaa     1280
ttcatgatgt taactccatg gtaagtcaaa taggtaccaa aaaaataaaa ggaacaatta     1340
cacacagttc agtaagtatc attttgggtt tctccatgta aaaattaacc aatgaaataa     1400
aacatatcaa ctatagatga cctgatttca ggaaaaccac atttcaaaat tacaattaca     1460
ttattttcct catgtcatcc tcagtcattg acaggaattt tgtaggccac catgctattt     1520
actttgtgga ttgtagtagt aaatgaacga aggcgcactt cctcagaatt ggtaataaac     1580
tgtgtgcccc actcttccca tttttcaggt acaaccaaatt ctttgtctgt ataatcagc     1640
agatcaaattg aacaagaaac ttccaacagt ggcagaaatg tcaccgtagc tgtgatctgt     1700
ctgatcactg aacggatttc atcctggata gctttctgag acttttctct gggtgactg     1760
tcactctttg cagtcttgtc aactcaata tcaaactgcc atctttccag gacctacca     1820
ctttcaatat ttgagataac tacaaccagt ttctgaactg aacacttgta taaccaatct     1880
ttcagttggt ccaccacatt atttaggtat tttatgagct caagatcagt agttacaagc     1940
aaggtagtgc cgtattttct cactcgagta aaggtttcag atggatatat gccacgctga     2000
tataaaatgc tgttgatgcc gaatgagaag aactcgcca cgatttcggc gctcccgcc     2060
agggtgattc cctgctcccc ggagagctgc agcgccatgg ccaggggacac aaacaaaagc     2120
acgcgttcc a                                                    2131

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<210> 478  
 <211> 106  
 <212> PRT  
 <213> Homo sapiens

<400> 478  
 Met Met Gly Val Leu Phe Cys Cys Gly Ala Gly Phe Phe Ile Arg Arg  
 1 5 10 15  
 Arg Met Tyr Pro Pro Pro Leu Ile Glu Glu Pro Ala Phe Asn Val Ser

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      20      25      30
Tyr Thr Arg Gln Pro Pro Asn Pro Gly Pro Gly Ala Gln Gln Pro Gly
      35      40      45
Pro Pro Tyr Tyr Thr Asp Pro Gly Gly Pro Gly Met Asn Pro Val Gly
      50      55      60
Asn Ser Met Ala Met Ala Phe Gln Val Pro Pro Asn Ser Pro Gln Gly
      65      70      75      80
Ser Val Ala Cys Pro Pro Pro Pro Ala Tyr Cys Asn Thr Pro Pro Pro
      85      90      95
Pro Tyr Glu Gln Val Val Lys Ala Lys *
      100      105

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<210> 479  
 <211> 739  
 <212> PRT  
 <213> Homo sapiens

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      <400> 479
Met Thr Ser Asp Gln Asp Ala Lys Val Val Ala Glu Pro Gln Thr Gln
  1      5      10      15
Arg Val Gln Glu Gly Lys Asp Ser Ala His Leu Met Asn Gly Pro Ile
      20      25      30
Ser Gln Thr Thr Ser Gln Thr Ser Ser Ile Pro Pro Leu Ser Gln Val
      35      40      45
Pro Ala Thr Lys Val Ser Glu Leu Asn Pro Asn Ala Glu Val Trp Gly
      50      55      60
Ala Pro Val Leu His Leu Glu Ala Ser Ser Ala Ala Asp Gly Val Ser
      65      70      75      80
Ala Ala Trp Glu Glu Val Ala Gly His His Ala Asp Arg Gly Pro Gln
      85      90      95
Gly Ser Asp Ala Asn Gly Asp Gly Asp Gln Gly His Glu Asn Ala Ala
      100      105      110
Leu Pro Asp Pro Gln Glu Ser Asp Pro Ala Asp Met Asn Ala Leu Ala
      115      120      125
Leu Gly Pro Ser Glu Tyr Asp Ser Leu Pro Glu Asn Ser Glu Thr Gly
      130      135      140
Gly Asn Glu Ser Gln Pro Asp Ser Gln Glu Asp Pro Arg Glu Val Leu
      145      150      155      160
Lys Lys Thr Leu Glu Phe Cys Leu Ser Arg Glu Asn Leu Ala Ser Asp
      165      170      175
Met Tyr Leu Ile Ser Gln Met Asp Ser Asp Gln Tyr Val Pro Ile Thr
      180      185      190
Thr Val Ala Asn Leu Asp His Ile Lys Lys Leu Ser Thr Asp Val Asp
      195      200      205
Leu Ile Val Glu Val Leu Arg Ser Leu Pro Leu Val Gln Val Asp Glu
      210      215      220
Lys Gly Glu Lys Val Arg Pro Asn Gln Asn Arg Cys Ile Val Ile Leu
      225      230      235      240
Arg Glu Ile Ser Glu Ser Thr Pro Val Glu Glu Val Glu Ala Leu Phe
      245      250      255
Lys Gly Asp Asn Leu Pro Lys Phe Ile Asn Cys Glu Phe Ala Tyr Asn
      260      265      270
Asp Asn Trp Phe Ile Thr Phe Glu Thr Glu Ala Asp Ala Gln Gln Ala
      275      280      285
Tyr Lys Tyr Leu Arg Glu Glu Val Lys Thr Phe Gln Gly Lys Pro Ile
      290      295      300
Lys Ala Arg Ile Lys Ala Lys Ala Ile Ala Ile Asn Thr Phe Leu Pro
      305      310      315      320
Lys Asn Gly Phe Arg Pro Leu Asp Val Ser Leu Tyr Ala Gln Gln Arg
      325      330      335
Tyr Ala Thr Ser Phe Tyr Phe Pro Pro Met Tyr Ser Pro Gln Gln Gln

```

```

      340      345      350
Phe Pro Leu Tyr Ser Leu Ile Thr Pro Gln Thr Trp Ser Ala Thr His
      355      360      365
Ser Tyr Leu Asp Pro Pro Leu Val Thr Pro Phe Pro Asn Thr Gly Phe
      370      375      380
Ile Asn Gly Phe Thr Ser Pro Ala Phe Lys Pro Ala Ala Ser Pro Leu
385      390      395      400
Thr Ser Leu Arg Gln Tyr Pro Pro Arg Ser Arg Asn Pro Ser Lys Ser
      405      410      415
His Leu Arg His Ala Ile Pro Ser Ala Glu Arg Gly Pro Gly Leu Leu
      420      425      430
Glu Ser Pro Ser Ile Phe Asn Phe Thr Ala Asp Arg Leu Ile Asn Gly
      435      440      445
Val Arg Ser Pro Gln Thr Arg Gln Ala Gly Gln Thr Arg Thr Arg Ile
      450      455      460
Gln Asn Pro Ser Ala Tyr Ala Lys Arg Glu Ala Gly Pro Gly Arg Val
465      470      475      480
Glu Pro Gly Ser Leu Glu Ser Ser Pro Gly Leu Gly Arg Gly Arg Lys
      485      490      495
Asn Ser Phe Gly Tyr Arg Lys Lys Arg Glu Glu Lys Phe Thr Ser Ser
      500      505      510
Gln Thr Gln Ser Pro Thr Pro Pro Lys Pro Pro Ser Pro Ser Phe Glu
      515      520      525
Leu Gly Leu Ser Ser Phe Pro Pro Leu Pro Gly Ala Ala Gly Asn Leu
      530      535      540
Lys Thr Glu Asp Leu Phe Glu Asn Arg Leu Ser Ser Leu Ile Ile Gly
545      550      555      560
Pro Ser Lys Glu Arg Thr Leu Ser Ala Asp Ala Ser Val Asn Thr Leu
      565      570      575
Pro Val Val Val Ser Arg Glu Pro Ser Val Pro Ala Ser Cys Ala Val
      580      585      590
Ser Ala Thr Tyr Glu Arg Ser Pro Ser Pro Ala His Leu Pro Asp Asp
      595      600      605
Pro Lys Val Ala Glu Lys Gln Arg Glu Thr His Ser Val Asp Arg Leu
      610      615      620
Pro Ser Ala Leu Thr Ala Thr Ala Cys Lys Ser Val Gln Val Asn Gly
625      630      635      640
Ala Ala Thr Glu Leu Arg Lys Pro Ser Tyr Ala Glu Ile Cys Gln Arg
      645      650      655
Thr Ser Lys Glu Pro Pro Ser Ser Pro Leu Gln Pro Gln Lys Glu Gln
      660      665      670
Lys Pro Asn Thr Val Gly Cys Gly Lys Glu Glu Lys Lys Leu Ala Glu
      675      680      685
Pro Ala Glu Arg Tyr Arg Glu Pro Pro Ala Leu Lys Ser Thr Pro Gly
      690      695      700
Ala Pro Arg Asp Gln Arg Arg Pro Ala Gly Gly Arg Pro Ser Pro Ser
705      710      715      720
Ala Met Gly Lys Arg Leu Ser Arg Glu Gln Ser Thr Pro Pro Lys Ser
      725      730      735
Pro Gln *
738

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<210> 480
<211> 121
<212> PRT
<213> Homo sapiens

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      <400> 480
Met Gly Leu Ala Val Thr Phe Leu Ser Glu Thr Phe Leu Ser Ser Ala
  1              5              10              15
Gln Lys Arg Gly Arg Gly Gly Glu Ser Asp Leu Glu Pro Ile Asp Ser

```

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      20      25      30
Trp Leu Ile Thr Pro Gly Met Ile Pro Val Ala Gln Pro Ser Val Met
      35      40      45
Asp Asp Ile Glu Val Trp Leu Arg Thr Asp Leu Lys Gly Asp Asp Leu
      50      55      60
Glu Glu Gly Val Thr Ser Glu Glu Phe Asp Lys Phe Leu Glu Glu Arg
      65      70      75      80
Ala Lys Ala Ala Glu Met Val Pro Asp Leu Pro Ser Pro Pro Met Glu
      85      90      95
Ala Pro Ala Pro Ala Ser Asn Pro Ser Gly Arg Lys Lys Pro Glu Arg
      100      105      110
Ser Glu Asp Ala Leu Phe Ala Leu *
      115      120

```

&lt;210&gt; 481

&lt;211&gt; 374

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

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Met Leu Lys Arg Lys Pro Ser Asn Val Ser Glu Lys' Glu Lys His Gln
  1      5      10      15
Lys Pro Lys Arg Ser Ser Ser Phe Gly Asn Phe Asp Arg Phe Arg Asn
      20      25      30
Asn Ser Leu Ser Lys Pro Asp Asp Ser Thr Glu Ala His Glu Gly Asp
      35      40      45
Pro Thr Asn Gly Ser Gly Glu Gln Ser Lys Thr Ser Asn Asn Gly Gly
      50      55      60
Gly Leu Gly Lys Lys Met Arg Ala Ile Ser Trp Thr Met Lys Lys Lys
      65      70      75      80
Val Gly Lys Lys Tyr Ile Lys Ala Leu Ser Glu Glu Lys Asp Glu Glu
      85      90      95
Asp Gly Glu Asn Ala His Pro Tyr Arg Asn Ser Asp Pro Val Ile Gly
      100      105      110
Thr His Thr Glu Lys Val Ser Leu Lys Ala Ser Asp Ser Met Asp Ser
      115      120      125
Leu Tyr Ser Gly Gln Ser Ser Ser Ser Gly Ile Thr Ser Cys Ser Asp
      130      135      140
Gly Thr Ser Asn Arg Asp Ser Phe Arg Leu Asp Asp Asp Gly Pro Tyr
      145      150      155      160
Ser Gly Pro Phe Cys Gly Arg Ala Arg Val His Thr Asp Phe Thr Pro
      165      170      175
Ser Pro Tyr Asp Thr Asp Ser Leu Lys Ile Lys Lys Gly Asp Ile Ile
      180      185      190
Asp Ile Ile Cys Lys Thr Pro Met Gly Met Trp Thr Gly Met Leu Asn
      195      200      205
Asn Lys Val Gly Asn Phe Lys Phe Ile Tyr Val Asp Val Ile Ser Glu
      210      215      220
Glu Glu Ala Ala Pro Lys Lys Ile Lys Ala Asn Arg Arg Ser Asn Ser
      225      230      235      240
Lys Lys Ser Lys Thr Leu Gln Glu Phe Leu Glu Arg Ile His Leu Gln
      245      250      255
Glu Tyr Thr Ser Thr Leu Leu Leu Asn Gly Tyr Glu Thr Leu Glu Asp
      260      265      270
Leu Lys Asp Ile Lys Glu Ser His Leu Ile Glu Leu Asn Ile Glu Asn
      275      280      285
Pro Asp Asp Arg Arg Arg Leu Leu Ser Ala Ala Glu Asn Phe Leu Glu
      290      295      300
Glu Glu Ile Ile Gln Glu Glu Asn Glu Pro Glu Pro Leu Ser Leu
      305      310      315      320
Ser Ser Asp Ile Ser Leu Asn Lys Ser Gln Leu Asp Asp Cys Pro Arg

```

325 330 335  
 Asp Ser Gly Cys Tyr Ile Ser Ser Gly Asn Ser Asp Asn Gly Lys Glu  
 340 345 350  
 Asp Leu Glu Ser Glu Asn Leu Ser Asp Met Val His Lys Ile Ile Ile  
 355 360 365  
 Thr Glu Pro Ser Asp \*  
 370 373

<210> 482  
 <211> 429  
 <212> PRT  
 <213> Homo sapiens

<400> 482  
 Met Lys Leu Ser Ala Glu Ser Tyr Lys Glu Thr Gln Met Val Lys Ile  
 1 5 10 15  
 Lys Glu Glu Pro Met Glu Val Asp Ile Gln Asp Ser His Val Ser Ile  
 20 25 30  
 Ser Pro Ser Arg Asn Val Gly Tyr Ser Thr Leu Ile Gly Arg Glu Lys  
 35 40 45  
 Thr Glu Pro Leu Gln Lys Met Pro Glu Gly Arg Val Pro Pro Glu Arg  
 50 55 60  
 Asn Leu Phe Ser Gln Asp Ile Ser Val Lys Met Ala Ser Glu Leu Leu  
 65 70 75 80  
 Phe Gln Leu Ser Glu Lys Val Ser Lys Glu His Asn His Thr Lys Glu  
 85 90 95  
 Asn Thr Ile Arg Thr Thr Thr Ser Pro Phe Phe Ser Glu Asp Thr Phe  
 100 105 110  
 Arg Gln Ser Pro Phe Thr Ser Asn Ser Lys Glu Leu Leu Pro Ser Asp  
 115 120 125  
 Ser Val Leu His Gly Arg Ile Ser Ala Pro Glu Thr Glu Lys Ile Val  
 130 135 140  
 Leu Glu Ala Gly Asn Gly Leu Pro Ser Trp Lys Phe Asn Asp Gln Leu  
 145 150 155 160  
 Phe Pro Cys Asp Val Cys Gly Lys Val Phe Gly Arg Gln Gln Thr Leu  
 165 170 175  
 Ser Arg His Leu Ser Leu His Thr Glu Glu Arg Lys Tyr Lys Cys His  
 180 185 190  
 Leu Cys Pro Tyr Ala Ala Lys Cys Arg Ala Asn Leu Asn Gln His Leu  
 195 200 205  
 Thr Val His Ser Val Lys Leu Val Ser Thr Asp Thr Glu Asp Ile Val  
 210 215 220  
 Ser Ala Val Thr Ser Glu Gly Ser Asp Gly Lys Lys His Pro Tyr Tyr  
 225 230 235 240  
 Tyr Ser Cys His Val Cys Gly Phe Glu Thr Glu Leu Asn Val Gln Phe  
 245 250 255  
 Val Ser His Met Ser Leu His Val Asp Lys Glu Gln Trp Met Phe Ser  
 260 265 270  
 Ile Cys Cys Thr Ala Cys Asp Phe Val Thr Met Glu Glu Ala Glu Ile  
 275 280 285  
 Lys Thr His Ile Gly Thr Lys His Thr Gly Glu Asp Arg Lys Thr Pro  
 290 295 300  
 Ser Glu Ser Asn Ser Pro Ser Ser Ser Ser Leu Ser Ala Leu Ser Asp  
 305 310 315 320  
 Ser Ala Asn Ser Lys Asp Asp Ser Asp Gly Ser Gln Lys Asn Lys Gly  
 325 330 335  
 Gly Asn Asn Leu Leu Val Ile Ser Val Met Pro Gly Ser Gln Pro Ser  
 340 345 350  
 Leu Asn Ser Glu Glu Lys Pro Glu Lys Gly Phe Glu Cys Val Phe Cys  
 355 360 365  
 Asn Phe Val Cys Lys Thr Lys Asn Met Phe Glu Arg His Leu Gln Ile



370                      375                      380  
 His Leu Ile Thr Arg Met Phe Glu Cys Asp Val Cys His Lys Phe Met  
 385                      390                      395                      400  
 Lys Thr Pro Glu Gln Leu Leu Glu His Lys Lys Cys His Thr Val Pro  
                     405                      410                      415  
 Thr Gly Gly Leu Asn Leu Cys Ser Arg Met Thr Lys \*  
                     420                      425                      428

<210> 483  
 <211> 483  
 <212> PRT  
 <213> Homo sapiens

<400> 483  
 Met Gly Ser Arg His Phe Glu Gly Ile Tyr Asp His Val Gly His Phe  
 1                      5                      10                      15  
 Gly Arg Phe Gln Arg Val Leu Tyr Phe Ile Cys Ala Phe Gln Asn Ile  
                     20                      25                      30  
 Ser Cys Gly Ile His Tyr Leu Ala Ser Val Phe Met Gly Val Thr Pro  
                     35                      40                      45  
 His His Val Cys Arg Pro Pro Gly Asn Cys His Leu Asp Ser Leu Trp  
                     50                      55                      60  
 Asp Leu Gly Ile Arg Gly Pro Glu Thr Lys Met Leu Leu Pro Tyr Cys  
                     65                      70                      75                      80  
 Leu Leu Thr Lys Leu Gly Arg Arg Val Val Leu Trp Ala Thr Ser Ser  
                     85                      90                      95  
 Ser Met Phe Leu Phe Gly Ile Ala Ala Ala Phe Ala Val Asp Tyr Tyr  
                     100                      105                      110  
 Thr Phe Met Ala Ala Arg Phe Phe Leu Ala Met Val Ala Ser Gly Tyr  
                     115                      120                      125  
 Leu Val Val Gly Phe Val Tyr Val Met Glu Phe Ile Gly Met Lys Ser  
                     130                      135                      140  
 Arg Thr Trp Ala Ser Val His Leu His Ser Phe Phe Ala Val Gly Thr  
                     145                      150                      155                      160  
 Leu Leu Val Ala Leu Thr Gly Tyr Leu Val Arg Thr Trp Trp Leu Tyr  
                     165                      170                      175  
 Gln Met Ile Leu Ser Thr Val Thr Val Pro Phe Ile Leu Cys Cys Trp  
                     180                      185                      190  
 Val Leu Pro Glu Thr Pro Phe Trp Leu Leu Ser Glu Gly Arg Tyr Glu  
                     195                      200                      205  
 Glu Ala Gln Lys Ile Val Asp Ile Met Ala Lys Trp Asn Arg Ala Ser  
                     210                      215                      220  
 Ser Cys Lys Leu Ser Glu Leu Leu Ser Leu Asp Leu Gln Gly Pro Val  
                     225                      230                      235                      240  
 Ser Asn Ser Pro Thr Glu Val Gln Lys His Asn Leu Ser Tyr Leu Phe  
                     245                      250                      255  
 Tyr Asn Trp Ser Ile Thr Lys Arg Thr Leu Thr Val Trp Leu Ile Trp  
                     260                      265                      270  
 Phe Thr Gly Ser Leu Gly Phe Tyr Ser Phe Ser Leu Asn Ser Val Asn  
                     275                      280                      285  
 Leu Gly Gly Asn Glu Tyr Leu Asn Leu Phe Leu Leu Gly Val Val Glu  
                     290                      295                      300  
 Ile Pro Ala Tyr Thr Phe Val Cys Ile Ala Met Asp Lys Val Gly Arg  
                     305                      310                      315                      320  
 Arg Thr Val Leu Ala Tyr Ser Leu Phe Cys Ser Ala Leu Ala Cys Gly  
                     325                      330                      335  
 Val Val Met Val Ile Pro Gln Lys His Tyr Ile Leu Gly Val Val Thr  
                     340                      345                      350  
 Ala Met Val Gly Lys Phe Ala Ile Gly Ala Ala Phe Gly Leu Ile Tyr  
                     355                      360                      365  
 Leu Tyr Thr Ala Glu Leu Tyr Pro Thr Ile Val Arg Ser Leu Ala Val

370 375 380  
 Gly Ser Gly Ser Met Val Cys Arg Leu Ala Ser Ile Leu Ala Pro Phe  
 385 390 395 400  
 Ser Val Asp Leu Ser Ser Ile Trp Ile Phe Ile Pro Gln Leu Phe Val  
 405 410 415  
 Gly Thr Met Ala Leu Leu Ser Gly Val Leu Thr Leu Lys Leu Pro Glu  
 420 425 430  
 Thr Leu Gly Lys Arg Leu Ala Thr Thr Trp Glu Glu Ala Ala Lys Leu  
 435 440 445  
 Glu Ser Glu Asn Glu Ser Lys Ser Ser Lys Leu Leu Leu Thr Thr Asn  
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 <213> Homo sapiens

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 Val Asp Leu Ile Arg Gly Ser Thr Phe Ala Lys Ala Lys Pro Glu Ile  
 50 55 60  
 Pro Trp Thr Ser Leu Thr Arg Lys Gly Leu Val Arg Val Val Phe Phe  
 65 70 75 80  
 Pro Leu Phe Ser Asn Trp Trp Ile Gln Val Thr Ser Leu Arg Ile Phe  
 85 90 95  
 Val Trp Leu Leu Leu Tyr Phe Met Gln Val Ile Ala Ile Val Leu  
 100 105 110  
 Tyr Leu Met Met Pro Ile Val Asn Ile Ser Glu Val Leu Gly Pro Leu  
 115 120 125  
 Cys Leu Met Leu Leu Met Gly Thr Val His Cys Gln Ile Val Ser Thr  
 130 135 140  
 Gln Ile Thr Arg Pro Ser Gly Asn Asn Gly Asn Arg Arg Arg Arg Lys  
 145 150 155 160  
 Leu Arg Lys Thr Val Asn Gly Asp Gly Ser Arg Glu Asn Gly Asn Asn  
 165 170 175  
 Ser Ser Asp Lys Val Arg Gly Ile Glu Thr Leu Glu Ser Val Pro Ile  
 180 185 190  
 Ile Gly Gly Phe Trp Glu Thr Ile Phe Gly Asn Arg Ile Lys Arg Val  
 195 200 205  
 Lys Leu Ile Ser Asn Lys Gly Thr Glu Thr Asp Asn Asp Pro Ser Cys  
 210 215 220  
 Val His Pro Ile Ile Lys Arg Arg Gln Cys Arg Pro Glu Ile Arg Met  
 225 230 235 240  
 Cys Gln Thr Arg Glu Lys Pro Lys Phe Ser Asp Gly Glu Lys Cys Arg  
 245 250 255  
 Arg Glu Ala Phe Arg Arg Leu Gly Asn Gly Val Ser Asp Asp Leu Ser  
 260 265 270  
 Ser Glu Glu Asp Gly Glu Ala Arg Thr Gln Met Ile Leu Leu Arg Arg  
 275 280 285  
 Ser Val Glu Gly Ala Ser Ser Asp Asn Gly Cys Glu Val Lys Asn Arg  
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 Lys Ser Ile Leu Ser Arg His Leu Asn Ser Gln Val Lys Lys Thr Thr

WO 01/53453

PCT/US00/34960

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Thr Arg Trp Cys His Ile Val Arg Asp Ser Asp Ser Leu Ala Glu Ser
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Glu Phe Glu Ser Ala Ala Phe Ser Gln Gly Ser Arg Ser Gly Val Ser
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Arg His Asp Ser Glu Thr Glu Asp Met Leu Trp Asp Asp Leu Leu His
          370          375          380
Gly Pro Glu Cys Arg Ser Ser Val Thr Ser Asp Ser Glu Gly Ala His
385          390          395          400
Val Asn Thr Leu His Ser Gly Thr Lys Arg Asp Pro Lys Glu Asp Val
          405          410          415
Phe Gln Gln Asn His Leu Phe Trp Leu Gln Asn Ser Ser Pro Ser Ser
          420          425          430
Asp Arg Val Ser Ala Ile Ile Trp Glu Gly Asn Glu Cys Lys Lys Met
          435          440          445
Asp Met Ser Val Leu Glu Ile Ser Gly Ile Ile Met Ser Arg Val Asn
          450          455          460
Ala Tyr Gln Gln Gly Val Gly Tyr Gln Met Leu Gly Asn Val Val Thr
465          470          475          480
Ile Gly Leu Ala Phe Phe Pro Phe Leu His Arg Leu Phe Arg Glu Lys
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Ser Leu Asp Gln Leu Lys Ser Ile Ser Ala Glu Glu Ile Leu Thr Leu
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Phe Cys Gly Ala Pro Pro Val Thr Pro Ile Ile Val Leu Ser Ile Ile
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Asn Phe Phe Glu Arg Leu Cys Leu Thr Trp Met Phe Phe Phe Met Met
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Cys Val Ala Glu Arg Thr Tyr Lys Gln Arg Phe Leu Phe Ala Lys Leu
545          550          555          560
Phe Ser His Ile Thr Ser Ala Arg Lys Ala Arg Lys Tyr Glu Ile Pro
          565          570          575
His Phe Arg Leu Lys Lys Val Glu Asn Ile Lys Ile Trp Leu Ser Leu
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Arg Ser Tyr Leu Lys Arg Arg Gly Pro Gln Arg Ser Val Asp Val Val
          595          600          605
Val Ser Ser Val Phe Leu Leu Thr Leu Ser Ile Ala Phe Ile Cys Cys
          610          615          620
Ala Gln Val Leu Gln Gly His Lys Thr Phe Leu Asn Asp Ala Tyr Asn
625          630          635          640
Trp Glu Phe Leu Ile Trp Glu Thr Ala Leu Leu Leu Phe Leu Leu Arg
          645          650          655
Leu Ala Ser Leu Gly Ser Glu Thr Asn Lys Lys Tyr Ser Asn Val Ser
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Ile Leu Leu Thr Glu Gln Ile Asn Leu Tyr Leu Lys Met Glu Lys Lys
          675          680          685
Pro Asn Lys Lys Glu Gln Leu Thr Leu Val Asn Asn Val Leu Lys Leu
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Ser Thr Lys Leu Leu Lys Glu Leu Asp Thr Pro Phe Arg Leu Tyr Gly
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Leu Thr Met Asn Pro Leu Ile Tyr Asn Ile Thr Arg Val Val Ile Leu
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Leu Trp Lys Ile Lys Ser *
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<213> Homo sapiens

<400> 485

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 Met Leu Leu Leu Met Ser Asp Asn Val Asp Arg Cys Phe Glu Thr Cys  
 35 40 45  
 Pro Pro Arg Thr Phe Leu Pro Ala Leu Cys Lys Ile Phe Leu Asp Glu  
 50 55 60  
 Ser Ala Pro Asp Asn Val Leu Glu Val Thr Ala Arg Ala Ile Thr Tyr  
 65 70 75 80  
 Tyr Leu Asp Val Ser Ala Glu Cys Thr Arg Arg Ile Val Gly Val Asp  
 85 90 95  
 Gly Ala Ile Lys Ala Leu Cys Asn Arg Leu Val Val Val Glu Leu Asn  
 100 105 110  
 Asn Arg Thr Ser Arg Asp Leu Ala Glu Gln Cys Val Lys Val Leu Glu  
 115 120 125  
 Leu Ile Cys Thr Arg Glu Ser Gly Ala Val Phe Glu Ala Gly Gly Leu  
 130 135 140  
 Asn Cys Val Leu Thr Phe Ile Arg Asp Ser Gly His Leu Val His Lys  
 145 150 155 160  
 Asp Thr Leu His Ser Ala Met Ala Val Val Ser Arg Leu Cys Gly Lys  
 165 170 175  
 Met Glu Pro Gln Asp Ser Ser Leu Glu Ile Cys Val Glu Ser Leu Ser  
 180 185 190  
 Ser Leu Leu Lys His Glu Asp His Gln Val Ser Asp Gly Ala Leu Arg  
 195 200 205  
 Cys Phe Ala Ser Leu Ala Asp Arg Phe Thr Arg Arg Gly Val Asp Pro  
 210 215 220  
 Ala Pro Leu Ala Lys His Gly Leu Thr Glu Glu Leu Leu Ser Arg Met  
 225 230 235 240  
 Ala Ala Ala Gly Gly Thr Val Ser Gly Pro Ser Ser Ala Cys Lys Pro  
 245 250 255  
 Gly Arg Ser Thr Thr Gly Ala Pro Ser Thr Thr Ala Asp Ser Lys Leu  
 260 265 270  
 Ser Asn Gln Val Ser Thr Ile Asp Leu Leu Arg Ser Glu Leu Pro Asp  
 275 280 285  
 Ser Ile Glu Ser Ala Leu Gln Gly Asp Glu Arg Cys Val Leu Asp Thr  
 290 295 300  
 Met Arg Leu Val Asp Leu Leu Leu Val Leu Leu Phe Glu Gly Arg Lys  
 305 310 315 320  
 Ala Leu Pro Lys Ser Ser Ala Gly Ser Thr Gly Arg Ile Pro Gly Leu  
 325 330 335  
 Arg Arg Leu Asp Ser Ser Gly Glu Arg Ser His Arg Gln Leu Ile Asp  
 340 345 350  
 Cys Ile Arg Ser Lys Asp Thr Asp Ala Leu Ile Asp Ala Ile Asp Thr  
 355 360 365  
 Gly Ala Phe Glu Val Asn Phe Met Asp Asp Val Gly Gln Thr Leu Leu  
 370 375 380  
 Asn Trp Ala Ser Ala Phe Gly Thr Gln Glu Met Val Glu Phe Leu Cys  
 385 390 395 400  
 Glu Arg Gly Ala Asp Val Asn Arg Gly Gln Arg Ser Ser Ser Leu His  
 405 410 415  
 Tyr Ala Ala Cys Phe Gly Arg Pro Gln Val Ala Lys Thr Leu Leu Arg  
 420 425 430  
 His Gly Ala Asn Pro Asp Leu Arg Asp Glu Asp Gly Lys Thr Pro Leu  
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 Asp Lys Ala Arg Glu Arg Gly His Ser Glu Val Val Ala Ile Leu Gln  
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 Ser Pro Gly Asp Trp Met Cys Pro Val Asn Lys Gly Asp Asp Lys Lys  
 465 470 475 480

Lys Lys Asp Thr Asn Lys Asp Glu Glu Glu Cys Asn Glu Pro Lys Gly  
 485 490 495  
 Asp Pro Glu Met Ala Pro Ile Tyr Leu Lys Arg Leu Leu Pro Val Phe  
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 Leu Ala Leu Ile Arg Lys Met Ile His Phe Cys Ser Glu Ala Leu Leu  
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 Lys Glu Val Cys Asp Ser Asp Val Gly His Asn Leu Pro Thr Ile Leu  
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 Val Glu Ile Thr Ala Thr Val Leu Asp Gln Glu Asp Asp Asp Asp Gly  
 565 570 575  
 His Leu Leu Ala Leu Gln Ile Ile Arg Asp Leu Val Asp Lys Gly Gly  
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 595 600 605  
 Ser Thr Leu Ala Gly Pro Ser Ser Asp Asp Glu Asn Glu Glu Glu Ser  
 610 615 620  
 Lys Pro Glu Lys Glu Asp Glu Pro Gln Glu Asp Ala Lys Glu Leu Gln  
 625 630 635 640  
 Gln Gly Lys Pro Tyr His Trp Arg Asp Trp Ser Ile Ile Arg Gly Arg  
 645 650 655  
 Asp Cys Leu Tyr Ile Trp Ser Asp Ala Ala Ala Leu Glu Leu Ser Asn  
 660 665 670  
 Gly Ser Asn Gly Trp Phe Arg Phe Ile Leu Asp Gly Lys Leu Ala Thr  
 675 680 685  
 Met Tyr Ser Ser Gly Ser Pro Glu Gly Gly Ser Asp Ser Ser Glu Ser  
 690 695 700  
 Arg Ser Glu Phe Leu Glu Lys Leu Gln Arg Ala Arg Gly Gln Val Lys  
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 Pro Ser Thr Ser Ser Gln Pro Ile Leu Ser Ala Pro Gly Pro Thr Lys  
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 Ala Ile His Asn Ser Asp Gly Gln Gln Ala Thr Ile Leu Lys Glu Asp  
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 Leu Pro Gly Phe Val Phe Glu Ser Asn Arg Gly Thr Lys His Ser Phe  
 770 775 780  
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 Val Arg Thr Met Ala Arg Asp Leu Tyr Asp Asp His Phe Lys Ala Val  
 820 825 830  
 Glu Ser Met Pro Arg Gly Val Val Val Thr Leu Arg Asn Ile Ala Thr  
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 Gln Leu Glu Ser Ser Trp Glu Leu His Thr Asn Arg Gln Cys Ile Glu  
 850 855 860  
 Ser Glu Asn Thr Trp Arg Asp Leu Met Lys Thr Ala Leu Glu Asn Leu  
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 885 890 895  
 Ser Ser Gly Leu Val Gln Ala Leu Leu Thr Val Leu Asn Asn Ser Met  
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 Asp Leu Asp Met Lys Gln Asp Cys Ser Gln Leu Val Glu Arg Ile Asn  
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 Val Phe Lys Thr Ala Phe Ser Glu Asn Glu Asp Asp Glu Ser Arg Pro  
 930 935 940  
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 Arg Leu Pro Leu His Leu Tyr Asp Thr Pro Gly Ser Thr Tyr Asn Leu  
 965 970 975  
 Gln Ile Leu Thr Arg Arg Leu Arg Phe Arg Leu Glu Arg Ala Pro Gly

980 985 990  
 Glu Thr Ala Leu Ile Asp Arg Thr Gly Arg Met Leu Lys Met Glu Pro  
 995 1000 1005  
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 Lys Gln Trp Tyr Asp Phe Asp Arg Ser Ser Phe Val Phe Val Arg Lys  
 1025 1030 1035 1040  
 Leu Arg Glu Gly Gln Asn Phe Ile Phe Arg His Gln His Asp Phe Asp  
 1045 1050 1055  
 Glu Asn Gly Ile Ile Tyr Trp Ile Gly Thr Asn Ala Lys Thr Ala Tyr  
 1060 1065 1070  
 Glu Trp Val Asn Pro Ala Ala Tyr Gly Leu Val Val Val Thr Ser Ser  
 1075 1080 1085  
 Glu Gly Arg Asn Leu Pro Tyr Gly Arg Leu Glu Asp Ile Leu Ser Arg  
 1090 1095 1100  
 Asp Asn Ser Ala Leu Asn Cys His Ser Asn Asp Asp Lys Asn Ala Trp  
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 Phe Ala Ile Asp Leu Gly Leu Trp Val Ile Pro Ser Ala Tyr Thr Leu  
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 Arg His Ala Arg Gly Tyr Gly Arg Ser Ala Leu Arg Asn Trp Val Phe  
 1140 1145 1150  
 Gln Val Ser Lys Asp Gly Gln Asn Trp Thr Ser Leu Tyr Thr His Val  
 1155 1160 1165  
 Asp Asp Cys Ser Leu Asn Glu Pro Gly Ser Thr Ala Thr Trp Pro Leu  
 1170 1175 1180  
 Asp Pro Pro Lys Asp Glu Lys Gln Gly Trp Arg His Val Arg Ile Lys  
 1185 1190 1195 1200  
 Gln Met Gly Lys Asn Ala Ser Gly Gln Thr His Tyr Leu Ser Leu Ser  
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 Gly Phe Glu Leu Tyr Gly Thr Val Asn Gly Val Cys Glu Asp Gln Leu  
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 Gly Lys Ala Ala Lys Glu Ala Glu Ala Asn Leu Arg Arg Gln Arg Arg  
 1235 1240 1245  
 Leu Val Arg Ser Gln Val Leu Lys Tyr Met Val Pro Gly Ala Arg Val  
 1250 1255 1260  
 Ile Arg Gly Leu Asp Trp Lys Trp Arg Asp Gln Asp Gly Ser Pro Gln  
 1265 1270 1275 1280  
 Gly Glu Gly Thr Val Thr Gly Glu Leu His Asn Gly Trp Ile Asp Val  
 1285 1290 1295  
 Thr Trp Asp Ala Gly Gly Ser Asn Ser Tyr Arg Met Gly Ala Glu Gly  
 1300 1305 1310  
 Lys Phe Asp Leu Lys Leu Ala Pro Gly Tyr Asp Pro Asp Thr Val Ala  
 1315 1320 1325  
 Ser Pro Lys Pro Val Ser Ser Thr Val Ser Gly Thr Thr Gln Ser Trp  
 1330 1335 1340  
 Ser Ser Leu Val Lys Asn Asn Cys Pro Asp Lys Thr Ser Ala Ala Ala  
 1345 1350 1355 1360  
 Gly Ser Ser Ser Arg Lys Gly Ser Ser Ser Val Cys Ser Val Ala  
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 Ser Ser Ser Asp Ile Ser Leu Gly Ser Thr Lys Thr Glu Arg Arg Ser  
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 1395 1400 1405  
 Pro Ile Val Val Leu Ser Ser Ala Glu Asn Val Pro Gln Thr Glu Val  
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 Gly Ser Ser Ser Ser Ala Ser Thr Ser Thr Leu Thr Ala Glu Thr Gly  
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 Ser Glu Asn Ala Glu Arg Lys Leu Gly Pro Asp Ser Ser Val Arg Thr  
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 Pro Gly Glu Ser Ser Ala Ile Ser Met Gly Ile Val Ser Val Ser Ser  
 1460 1465 1470  
 Pro Asp Val Ser Ser Val Ser Glu Leu Thr Asn Lys Glu Ala Ala Ser  
 1475 1480 1485

Gln Arg Pro Leu Ser Ser Ser Ala Ser Asn Arg Leu Ser Val Ser Ser  
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 Thr Ala Thr Ser Pro Leu Met Gly Ala Gln Ser Phe Pro Asn Leu Thr  
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 Thr Pro Gly Thr Thr Ser Thr Val Thr Met Ser Thr Ser Ser Val Thr  
 1585 1590 1595 1600  
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 Leu Pro Glu Pro Asp Glu Glu Asp Asp Glu Asn Glu Asp Asp Asn Gln  
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 Glu Asp Gln Glu Tyr Glu Glu Val Met Ile Leu Arg Arg Pro Ser Leu  
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 Gln Arg Arg Ala Gly Ser Arg Ser Asp Val Thr His His Ala Val Thr  
 1700 1705 1710  
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 1765 1770 1775  
 Leu Glu Ile Pro Pro Gly Thr Pro His Ser Glu Leu Leu Glu Glu  
 1780 1785 1790  
 Val Glu Cys Thr Pro Ser Pro Arg Leu Ala Leu Thr Leu Lys Val Thr  
 1795 1800 1805  
 Gly Leu Gly Thr Thr Arg Glu Val Glu Leu Pro Leu Thr Asn Phe Arg  
 1810 1815 1820  
 Ser Thr Ile Phe Tyr Tyr Val Gln Lys Leu Leu Gln Leu Ser Cys Asn  
 1825 1830 1835 1840  
 Gly Asn Val Lys Ser Asp Lys Leu Arg Arg Ile Trp Glu Pro Thr Tyr  
 1845 1850 1855  
 Thr Ile Met Tyr Arg Glu Met Lys Asp Ser Asp Lys Glu Lys Glu Asn  
 1860 1865 1870  
 Gly Lys Met Gly Cys Trp Ser Ile Glu His Val Glu Gln Tyr Leu Gly  
 1875 1880 1885  
 Thr Asp Glu Leu Pro Lys Asn Asp Leu Ile Thr Tyr Leu Gln Lys Asn  
 1890 1895 1900  
 Ala Asp Ala Ala Phe Leu Arg His Trp Lys Leu Thr Gly Thr Asn Lys  
 1905 1910 1915 1920  
 Ser Ile Arg Lys Asn Arg Asn Cys Ser Gln Leu Ile Ala Ala Tyr Lys  
 1925 1930 1935  
 Asp Phe Cys Glu His Gly Thr Lys Ser Gly Leu Asn Gln Gly Ala Ile  
 1940 1945 1950  
 Ser Thr Leu Gln Ser Ser Asp Ile Leu Asn Leu Thr Lys Glu Gln Pro  
 1955 1960 1965  
 Gln Ala Lys Ala Gly Asn Gly Gln Asn Ser Cys Gly Val Glu Asp Val  
 1970 1975 1980  
 Leu Gln Leu Leu Arg Ile Leu Tyr Ile Val Ala Ser Asp Pro Tyr Ser

1985	1990	1995	2000
Arg Ile Ser Gln Glu Asp Gly Asp Glu Gln Pro Gln Phe Thr Phe Pro			
	2005	2010	2015
Pro Asp Glu Phe Thr Ser Lys Lys Ile Thr Thr Lys Ile Leu Gln Gln			
	2020	2025	2030
Ile Glu Glu Pro Leu Ala Leu Ala Ser Gly Ala Leu Pro Asp Trp Cys			
	2035	2040	2045
Glu Gln Leu Thr Ser Lys Cys Pro Phe Leu Ile Pro Phe Glu Thr Arg			
	2050	2055	2060
Gln Leu Tyr Phe Thr Cys Thr Ala Phe Gly Ala Ser Arg Ala Ile Val			
2065	2070	2075	2080
Trp Leu Gln Asn Arg Arg Glu Ala Thr Val Glu Arg Thr Arg Thr Thr			
	2085	2090	2095
Ser Ser Val Arg Arg Asp Asp Pro Gly Glu Phe Arg Val Gly Arg Leu			
	2100	2105	2110
Lys His Glu Arg Val Lys Val Pro Arg Gly Glu Ser Leu Met Glu Trp			
	2115	2120	2125
Ala Glu Asn Val Met Gln Ile His Ala Asp Arg Lys Ser Val Leu Glu			
	2130	2135	2140
Val Glu Phe Leu Gly Glu Glu Gly Thr Gly Leu Gly Pro Thr Leu Glu			
2145	2150	2155	2160
Phe Tyr Ala Leu Val Ala Ala Glu Phe Gln Arg Thr Asp Leu Gly Ala			
	2165	2170	2175
Trp Leu Cys Asp Asp Asn Phe Pro Asp Asp Glu Ser Arg His Val Asp			
	2180	2185	2190
Leu Gly Gly Gly Leu Lys Pro Pro Gly Tyr Tyr Val Gln Arg Ser Cys			
	2195	2200	2205
Gly Leu Phe Thr Ala Pro Phe Pro Gln Asp Ser Asp Glu Leu Glu Arg			
	2210	2215	2220
Ile Thr Lys Leu Phe His Phe Leu Gly Ile Phe Leu Ala Lys Cys Ile			
2225	2230	2235	2240
Gln Asp Asn Arg Leu Val Asp Leu Pro Ile Ser Lys Pro Phe Phe Lys			
	2245	2250	2255
Leu Met Cys Met Gly Asp Ile Lys Ser Asn Met Ser Lys Leu Ile Tyr			
	2260	2265	2270
Glu Ser Arg Gly Asp Arg Asp Leu His Cys Thr Glu Ser Gln Ser Glu			
	2275	2280	2285
Ala Ser Thr Glu Glu Gly His Asp Ser Leu Ser Val Gly Ser Phe Glu			
	2290	2295	2300
Glu Asp Ser Lys Ser Glu Phe Ile Leu Asp Pro Pro Lys Pro Lys Pro			
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Pro Ala Trp Phe Asn Gly Ile Leu Thr Trp Glu Asp Phe Glu Leu Val			
	2325	2330	2335
Asn Pro His Arg Ala Arg Phe Leu Lys Glu Ile Lys Asp Leu Ala Ile			
	2340	2345	2350
Lys Arg Arg Gln Ile Leu Ser Asn Lys Gly Leu Ser Glu Asp Glu Lys			
	2355	2360	2365
Asn Thr Lys Leu Gln Glu Leu Val Leu Lys Asn Pro Ser Gly Ser Gly			
	2370	2375	2380
Pro Pro Leu Ser Ile Glu Asp Leu Gly Leu Asn Phe Gln Phe Cys Pro			
2385	2390	2395	2400
Ser Ser Arg Ile Tyr Gly Phe Thr Ala Val Asp Leu Lys Pro Ser Gly			
	2405	2410	2415
Glu Asp Glu Met Ile Thr Met Asp Asn Ala Glu Glu Tyr Val Asp Leu			
	2420	2425	2430
Met Phe Asp Phe Cys Met His Thr Gly Ile Gln Lys Gln Met Glu Ala			
	2435	2440	2445
Phe Arg Asp Gly Phe Asn Lys Val Phe Pro Met Glu Lys Leu Ser Ser			
	2450	2455	2460
Phe Ser His Glu Glu Val Gln Met Ile Leu Cys Gly Asn Gln Ser Pro			
2465	2470	2475	2480
Ser Trp Ala Ala Glu Asp Ile Ile Asn Tyr Thr Glu Pro Lys Leu Gly			
	2485	2490	2495



Tyr Thr Arg Asp Ser Pro Gly Phe Leu Arg Phe Val Arg Val Leu Cys  
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 Gly Met Ser Ser Asp Glu Arg Lys Ala Phe Leu Gln Phe Thr Thr Gly  
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 Cys Ser Thr Leu Pro Pro Gly Gly Leu Ala Asn Leu His Pro Arg Leu  
                   2530                  2535                  2540  
 Thr Val Val Arg Lys Val Asp Ala Thr Asp Ala Ser Tyr Pro Ser Val  
 2545                  2550                  2555                  2560  
 Asn Thr Cys Val His Tyr Leu Lys Leu Pro Glu Tyr Ser Ser Glu Glu  
                   2565                  2570                  2575  
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                   50                  55                  60  
 Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met Trp Asn Leu Ala Gly  
                   65                  70                  75                  80  
 Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe Thr Gln Thr Ala Val  
                   85                  90                  95  
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                   100                  105                  110  
 Pro Phe Lys Arg Thr Pro Pro Asn Phe Gln Ser Gln Asp Tyr Val Glu  
                   115                  120                  125  
 Leu Thr Phe Glu Gln Gln Val Tyr Pro Thr Ala Val His Val Leu Glu  
                   130                  135                  140  
 Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu Ala Cys Ser Ala Asn  
                   145                  150                  155                  160  
 Pro Tyr Ser Pro Asn Pro Pro Ala Glu Val Arg Trp Glu Ile Leu Trp  
                   165                  170                  175  
 Ser Glu Arg Pro Thr Lys Val Asn Ala Ser Gln Ala Arg Gln Phe Lys  
                   180                  185                  190  
 Pro Cys Ile Lys Gln Ile Asn Phe Pro Thr Asn Leu Ile Arg Leu Glu  
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 Val Asn Ser Ser Leu Leu Glu Tyr Tyr Thr Glu Leu Asp Ala Val Val  
                   210                  215                  220  
 Leu His Gly Val Lys Asp Lys Pro Val Leu Ser Leu Lys Thr Ser Leu  
                   225                  230                  235                  240  
 Ile Asp Met Asn Asp Ile Glu Asp Asp Ala Tyr Ala Glu Lys Asp Gly  
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 Cys Gly Met Asp Ser Leu Asn Lys Lys Phe Ser Ser Ala Val Leu Gly  
                   260                  265                  270  
 Glu Gly Pro Asn Asn Gly Tyr Phe Asp Lys Leu Pro Tyr Glu Leu Ile  
                   275                  280                  285  
 Gln Leu Ile Leu Asn His Leu Thr Leu Pro Asp Leu Cys Arg Leu Ala  
                   290                  295                  300  
 Gln Thr Cys Lys Leu Leu Ser Gln His Cys Cys Asp Pro Leu Gln Tyr  
                   305                  310                  315                  320

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Ile His Leu Asn Leu Gln Pro Tyr Trp Ala Lys Leu Asp Asp Thr Ser
      325      330      335
Leu Glu Phe Leu Gln Ser Arg Cys Thr Leu Val Gln Trp Leu Asn Leu
      340      345      350
Ser Trp Thr Gly Asn Arg Gly Phe Ile Ser Val Ala Gly Phe Ser Arg
      355      360      365
Phe Leu Lys Val Cys Gly Ser Glu Leu Val Arg Leu Glu Leu Ser Cys
      370      375      380
Ser His Phe Leu Asn Glu Thr Cys Leu Glu Val Ile Ser Glu Met Cys
      385      390      395      400
Pro Asn Leu Gln Ala Leu Asn Leu Ser Ser Cys Asp Lys Leu Pro Pro
      405      410      415
Gln Ala Phe Asn His Ile Ala Lys Leu Cys Ser Leu Lys Arg Leu Val
      420      425      430
Leu Tyr Arg Thr Lys Val Glu Gln Thr Ala Leu Leu Ser Ile Leu Asn
      435      440      445
Phe Cys Ser Glu Leu Gln His Leu Ser Leu Gly Ser Cys Val Met Ile
      450      455      460
Glu Asp Tyr Asp Val Ile Ala Ser Met Ile Gly Ala Lys Cys Lys Lys
      465      470      475      480
Leu Arg Thr Leu Asp Leu Trp Arg Cys Lys Asn Ile Thr Glu Asn Gly
      485      490      495
Ile Ala Glu Leu Ala Ser Gly Cys Pro Leu Leu Glu Glu Leu Asp Leu
      500      505      510
Gly Trp Cys Pro Thr Leu Gln Ser Ser Thr Gly Cys Phe Thr Arg Leu
      515      520      525
Ala His Gln Leu Pro Asn Leu Gln Lys Leu Phe Leu Thr Ala Asn Arg
      530      535      540
Ser Val Cys Asp Thr Asp Ile Asp Glu Leu Ala Cys Asn Cys Thr Arg
      545      550      555      560
Leu Gln Gln Leu Asp Ile Leu Gly Thr Arg Met Val Ser Pro Ala Ser
      565      570      575
Leu Arg Lys Leu Glu Ser Cys Lys Asp Leu Ser Leu Leu Asp Val
      580      585      590
Ser Phe Cys Ser Gln Ile Asp Asn Arg Ala Val Leu Glu Leu Asn Ala
      595      600      605
Ser Phe Pro Lys Val Phe Ile Lys Lys Ser Phe Thr Gln *
      610      615      620 621

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<210> 487  
 <211> 598  
 <212> PRT  
 <213> Homo sapiens

```

<400> 487
Met Ser Pro Val Phe Pro Met Leu Thr Val Leu Thr Met Phe Tyr Tyr
  1      5      10      15
Ile Cys Leu Arg Arg Ala Arg Thr Ala Thr Arg Gly Glu Met Met
  20      25      30
Asn Thr His Arg Ala Ile Glu Ser Asn Ser Gln Thr Ser Pro Leu Asn
  35      40      45
Ala Glu Val Val Gln Tyr Ala Lys Glu Val Val Asp Phe Ser Ser His
  50      55      60
Tyr Gly Ser Glu Asn Ser Met Ser Tyr Thr Met Trp Asn Leu Ala Gly
  65      70      75      80
Val Pro Asn Val Phe Pro Ser Ser Gly Asp Phe Thr Gln Thr Ala Val
  85      90      95
Phe Arg Thr Tyr Gly Thr Trp Trp Asp Gln Cys Pro Ser Ala Ser Leu
  100     105     110
Pro Phe Lys Arg Thr Pro Pro Asn Phe Gln Ser Gln Asp Tyr Val Glu
  115     120     125

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Leu Thr Phe Glu Gln Gln Val Tyr Pro Thr Ala Val His Val Leu Glu  
 130 135 140  
 Thr Tyr His Pro Gly Ala Val Ile Arg Ile Leu Ala Cys Ser Ala Asn  
 145 150 155 160  
 Pro Tyr Ser Pro Asn Pro Pro Ala Glu Val Arg Trp Glu Ile Leu Trp  
 165 170 175  
 Ser Glu Arg Pro Thr Lys Val Asn Ala Ser Gln Ala Arg Gln Phe Lys  
 180 185 190  
 Pro Cys Ile Lys Gln Ile Asn Phe Pro Thr Asn Leu Ile Arg Leu Glu  
 195 200 205  
 Val Asn Ser Ser Leu Leu Glu Tyr Tyr Thr Glu Leu Asp Ala Val Val  
 210 215 220  
 Leu His Gly Val Lys Asp Lys Pro Val Leu Ser Leu Lys Thr Ser Leu  
 225 230 235 240  
 Ile Asp Met Asn Asp Ile Glu Asp Asp Ala Tyr Ala Glu Lys Asp Gly  
 245 250 255  
 Cys Gly Met Asp Ser Leu Asn Lys Lys Phe Ser Ser Ala Val Leu Gly  
 260 265 270  
 Glu Gly Pro Asn Asn Gly Tyr Phe Asp Lys Leu Pro Tyr Glu Leu Ile  
 275 280 285  
 Gln Leu Ile Leu Asn His Leu Thr Leu Pro Asp Leu Cys Arg Leu Ala  
 290 295 300  
 Gln Thr Cys Lys Leu Leu Ser Gln His Cys Cys Asp Pro Leu Gln Tyr  
 305 310 315 320  
 Ile His Leu Asn Leu Gln Pro Tyr Trp Ala Lys Leu Asp Asp Thr Ser  
 325 330 335  
 Leu Glu Phe Leu Gln Ser Arg Cys Thr Leu Val Gln Trp Leu Asn Leu  
 340 345 350  
 Ser Trp Thr Gly Asn Arg Gly Phe Ile Ser Val Ala Gly Phe Ser Arg  
 355 360 365  
 Phe Leu Lys Val Cys Gly Ser Glu Leu Val Arg Leu Glu Leu Ser Cys  
 370 375 380  
 Ser His Phe Leu Asn Glu Thr Cys Leu Glu Val Ile Ser Glu Met Cys  
 385 390 395 400  
 Pro Asn Leu Gln Ala Leu Asn Leu Ser Ser Cys Asp Lys Leu Pro Pro  
 405 410 415  
 Gln Ala Phe Asn His Ile Ala Lys Leu Cys Ser Leu Lys Arg Leu Val  
 420 425 430  
 Leu Tyr Arg Thr Lys Val Glu Ile Glu Asp Tyr Asp Val Ile Ala Ser  
 435 440 445  
 Met Ile Gly Ala Lys Cys Lys Lys Leu Arg Thr Leu Asp Leu Trp Arg  
 450 455 460  
 Cys Lys Asn Ile Thr Glu Asn Gly Ile Ala Glu Leu Ala Ser Gly Cys  
 465 470 475 480  
 Pro Leu Leu Glu Glu Leu Asp Leu Gly Trp Cys Pro Thr Leu Gln Ser  
 485 490 495  
 Ser Thr Gly Cys Phe Thr Arg Leu Ala His Gln Leu Pro Asn Leu Gln  
 500 505 510  
 Lys Leu Phe Leu Thr Ala Asn Arg Ser Val Cys Asp Thr Asp Ile Asp  
 515 520 525  
 Glu Leu Ala Cys Asn Cys Thr Arg Leu Gln Gln Leu Asp Ile Leu Gly  
 530 535 540  
 Thr Arg Met Val Ser Pro Ala Ser Leu Arg Lys Leu Leu Glu Ser Cys  
 545 550 555 560  
 Lys Asp Leu Ser Leu Leu Asp Val Ser Phe Cys Ser Gln Ile Asp Asn  
 565 570 575  
 Arg Ala Val Leu Glu Leu Asn Ala Ser Phe Pro Lys Val Phe Ile Lys  
 580 585 590  
 Lys Ser Phe Thr Gln \*  
 595 597

&lt;211&gt; 984

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 488

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Met His Asn Leu Gln Thr Phe Leu Leu Asp Gly Asn Phe Leu Gln Ser
 1           5           10           15
Leu Pro Ala Glu Leu Glu Asn Met Lys Gln Leu Ser Tyr Leu Gly Leu
           20           25           30
Ser Phe Asn Glu Phe Thr Asp Ile Pro Glu Val Leu Glu Lys Leu Thr
           35           40           45
Ala Val Asp Lys Leu Cys Met Ser Gly Asn Cys Val Glu Thr Leu Arg
           50           55           60
Leu Gln Ala Leu Arg Lys Met Pro His Ile Lys His Val Asp Leu Arg
           65           70           75           80
Leu Asn Val Ile Arg Lys Leu Ile Ala Asp Glu Val Asp Phe Leu Gln
           85           90           95
His Val Thr Gln Leu Asp Leu Arg Asp Asn Lys Leu Gly Asp Leu Asp
           100          105          110
Ala Met Ile Phe Asn Asn Ile Glu Val Leu His Cys Glu Arg Asn Gln
           115          120          125
Leu Val Thr Leu Asp Ile Cys Gly Tyr Phe Leu Lys Ala Leu Tyr Ala
           130          135          140
Ser Ser Asn Glu Leu Val Gln Leu Asp Val Tyr Pro Val Pro Asn Tyr
           145          150          155          160
Leu Ser Tyr Met Asp Val Ser Arg Asn Arg Leu Glu Asn Val Pro Glu
           165          170          175
Trp Val Cys Glu Ser Arg Lys Leu Glu Val Leu Asp Ile Gly His Asn
           180          185          190
Gln Ile Cys Glu Leu Pro Ala Arg Leu Phe Cys Asn Ser Ser Leu Arg
           195          200          205
Lys Leu Leu Ala Gly His Asn Gln Leu Ala Arg Leu Pro Glu Arg Leu
           210          215          220
Glu Arg Thr Ser Val Glu Val Leu Asp Val Gln His Asn Gln Leu Leu
           225          230          235          240
Glu Leu Pro Pro Asn Leu Leu Met Lys Ala Asp Ser Leu Arg Phe Leu
           245          250          255
Asn Ala Ser Ala Asn Lys Leu Glu Ser Leu Pro Pro Ala Thr Leu Ser
           260          265          270
Glu Glu Thr Asn Ser Ile Leu Gln Glu Leu Tyr Leu Thr Asn Asn Ser
           275          280          285
Leu Thr Asp Lys Cys Val Pro Leu Leu Thr Gly His Pro His Leu Lys
           290          295          300
Ile Leu His Met Ala Tyr Asn Arg Leu Gln Ser Phe Pro Ala Ser Lys
           305          310          315          320
Met Ala Lys Leu Glu Glu Leu Glu Glu Ile Asp Leu Ser Gly Asn Lys
           325          330          335
Leu Lys Ala Ile Pro Thr Thr Ile Met Asn Cys Arg Arg Met His Thr
           340          345          350
Val Ile Ala His Ser Asn Cys Ile Glu Val Phe Pro Glu Val Met Gln
           355          360          365
Leu Pro Glu Ile Lys Cys Val Asp Leu Ser Cys Asn Glu Leu Ser Glu
           370          375          380
Val Thr Leu Pro Glu Asn Leu Pro Pro Lys Leu Gln Glu Leu Asp Leu
           385          390          395          400
Thr Gly Asn Pro Arg Leu Val Leu Asp His Lys Thr Leu Glu Leu Leu
           405          410          415
Asn Asn Ile Arg Cys Phe Lys Ile Asp Gln Pro Ser Thr Gly Asp Ala
           420          425          430
Ser Gly Ala Pro Ala Val Trp Ser His Gly Tyr Thr Glu Ala Ser Gly
           435          440          445
Val Lys Asn Lys Leu Cys Val Ala Ala Leu Ser Val Asn Asn Phe Cys

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450 455 460  
 Asp Asn Arg Glu Ala Leu Tyr Gly Val Phe Asp Gly Asp Arg Asn Val  
 465 470 475 480  
 Glu Val Pro Tyr Leu Leu Gln Cys Thr Met Ser Asp Ile Leu Ala Glu  
 485 490 495  
 Glu Leu Gln Lys Lys Thr Lys Asn Glu Glu Tyr Met Val Asn Thr  
 500 505 510  
 Phe Ile Val Met Gln Arg Lys Leu Gly Thr Ala Gly Gln Lys Leu Gly  
 515 520 525  
 Gly Ala Ala Val Leu Cys His Ile Lys His Asp Pro Val Asp Pro Gly  
 530 535 540  
 Gly Ser Phe Thr Leu Thr Ser Ala Asn Val Gly Lys Cys Gln Thr Val  
 545 550 555 560  
 Leu Cys Arg Asn Gly Lys Pro Leu Pro Leu Ser Arg Ser Tyr Ile Met  
 565 570 575  
 Ser Cys Glu Glu Glu Leu Lys Arg Ile Lys Gln His Lys Ala Ile Ile  
 580 585 590  
 Thr Glu Asp Gly Lys Val Asn Gly Val Thr Glu Ser Thr Arg Ile Leu  
 595 600 605  
 Gly Tyr Thr Phe Leu His Pro Ser Val Val Pro Arg Pro His Val Gln  
 610 615 620  
 Ser Val Leu Leu Thr Pro Gln Asp Glu Phe Phe Ile Leu Gly Ser Lys  
 625 630 635 640  
 Gly Leu Trp Asp Ser Leu Ser Val Glu Glu Ala Val Glu Ala Val Arg  
 645 650 655  
 Asn Val Pro Asp Ala Leu Ala Ala Ala Lys Lys Leu Cys Thr Leu Ala  
 660 665 670  
 Gln Ser Tyr Gly Cys His Asp Ser Ile Ser Ala Val Val Val Gln Leu  
 675 680 685  
 Ser Val Thr Glu Asp Ser Phe Cys Cys Cys Glu Leu Ser Ala Gly Gly  
 690 695 700  
 Ala Val Pro Pro Pro Ser Pro Gly Ile Phe Pro Pro Ser Val Asn Met  
 705 710 715 720  
 Val Ile Lys Asp Arg Pro Ser Asp Gly Leu Gly Val Pro Ser Ser Ser  
 725 730 735  
 Ser Gly Met Ala Ser Glu Ile Ser Ser Glu Leu Ser Thr Ser Glu Met  
 740 745 750  
 Ser Ser Glu Val Gly Ser Thr Ala Ser Asp Glu Pro Pro Gly Ala  
 755 760 765  
 Leu Ser Glu Asn Ser Pro Ala Tyr Pro Ser Glu Gln Arg Cys Met Leu  
 770 775 780  
 His Pro Ile Cys Leu Ser Asn Ser Phe Gln Arg Gln Leu Ser Ser Ala  
 785 790 795 800  
 Thr Phe Ser Ser Ala Phe Ser Asp Asn Gly Leu Asp Ser Asp Asp Glu  
 805 810 815  
 Glu Pro Ile Glu Gly Val Phe Thr Asn Gly Ser Arg Val Glu Val Glu  
 820 825 830  
 Val Asp Ile His Cys Ser Arg Ala Lys Glu Lys Glu Lys Gln Gln His  
 835 840 845  
 Leu Leu Gln Val Pro Ala Glu Ala Ser Asp Glu Gly Ile Val Ile Ser  
 850 855 860  
 Ala Asn Glu Asp Glu Pro Gly Leu Pro Arg Lys Ala Asp Phe Ser Ala  
 865 870 875 880  
 Val Gly Thr Ile Gly Arg Arg Arg Ala Asn Gly Ser Val Ala Pro Gln  
 885 890 895  
 Glu Arg Ser His Asn Val Ile Glu Val Ala Thr Asp Ala Pro Leu Arg  
 900 905 910  
 Lys Pro Gly Gly Tyr Phe Ala Ala Pro Ala Gln Pro Asp Pro Asp Asp  
 915 920 925  
 Gln Phe Ile Ile Pro Pro Glu Leu Glu Glu Glu Val Lys Glu Ile Met  
 930 935 940  
 Lys His His Gln Glu Gln Gln Gln Gln Gln Pro Pro Pro Pro Pro  
 945 950 955 960

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Gln Leu Gln Pro Gln Leu Pro Arg His Tyr Gln Leu Asp Gln Leu Pro  
 965 970 975  
 Asp Tyr Tyr Asp Thr Pro Leu \*  
 980 983

<210> 489  
 <211> 967  
 <212> PRT  
 <213> Homo sapiens

<400> 489  
 Met His Cys Ser Gly Leu Ala Trp His Pro Asp Ile Ala Thr Gln Leu  
 1 5 10 15  
 Val Leu Cys Ser Glu Asp Asp Arg Leu Pro Val Ile Gln Leu Trp Asp  
 20 25 30  
 Leu Arg Phe Ala Ser Ser Pro Leu Lys Val Leu Glu Ser His Ser Arg  
 35 40 45  
 Gly Ile Leu Ser Val Ser Trp Ser Gln Ala Asp Ala Glu Leu Leu Leu  
 50 55 60  
 Thr Ser Ala Lys Asp Ser Gln Ile Leu Cys Arg Asn Leu Gly Ser Ser  
 65 70 75 80  
 Glu Val Val Tyr Lys Leu Pro Thr Gln Ser Ser Trp Cys Phe Asp Val  
 85 90 95  
 Gln Trp Cys Pro Arg Asp Pro Ser Val Phe Ser Ala Ala Ser Phe Asn  
 100 105 110  
 Gly Trp Ile Ser Leu Tyr Ser Val Met Gly Arg Ser Trp Glu Val Gln  
 115 120 125  
 His Met Arg Gln Ala Asp Lys Ile Ser Ser Ser Phe Ser Lys Gly Gln  
 130 135 140  
 Pro Leu Pro Pro Leu Gln Val Pro Glu Gln Val Ala Gln Ala Pro Leu  
 145 150 155 160  
 Ile Pro Pro Leu Lys Lys Pro Pro Lys Trp Ile Arg Arg Pro Thr Gly  
 165 170 175  
 Val Ser Phe Ala Phe Gly Gly Lys Leu Val Thr Phe Gly Leu Pro Ser  
 180 185 190  
 Thr Pro Ala His Leu Val Pro Gln Pro Cys Pro Arg Leu Val Phe Ile  
 195 200 205  
 Ser Gln Val Thr Thr Glu Ser Glu Phe Leu Met Arg Ser Ala Glu Leu  
 210 215 220  
 Gln Glu Ala Leu Gly Ser Gly Asn Leu Leu Asn Tyr Cys Gln Asn Lys  
 225 230 235 240  
 Ser Gln Gln Ala Leu Leu Gln Ser Glu Lys Met Leu Trp Gln Phe Leu  
 245 250 255  
 Lys Val Thr Leu Glu Gln Asp Ser Arg Met Lys Phe Leu Lys Leu Leu  
 260 265 270  
 Gly Tyr Ser Lys Asp Glu Leu Gln Lys Lys Val Ala Thr Trp Leu Lys  
 275 280 285  
 Ser Asp Val Gly Leu Gly Glu Ser Pro Gln Pro Lys Gly Asn Asp Leu  
 290 295 300  
 Asn Ser Asp Arg Gln Gln Ala Phe Cys Ser Gln Ala Ser Lys His Thr  
 305 310 315 320  
 Thr Lys Glu Ala Ser Ala Ser Ser Ala Phe Phe Asp Glu Leu Val Pro  
 325 330 335  
 Gln Asn Met Thr Pro Trp Glu Ile Pro Ile Thr Lys Asp Ile Asp Gly  
 340 345 350  
 Leu Leu Ser Gln Ala Leu Leu Leu Gly Glu Leu Gly Pro Ala Val Glu  
 355 360 365  
 Leu Cys Leu Lys Glu Glu Arg Phe Ala Asp Ala Ile Ile Leu Ala Gln  
 370 375 380  
 Ala Gly Gly Thr Asp Leu Leu Lys Gln Thr Gln Glu Arg Tyr Leu Ala  
 385 390 395 400

Lys Lys Lys Thr Lys Ile Ser Ser Leu Leu Ala Cys Val Val Gln Lys  
 405 410 415  
 Asn Trp Lys Asp Val Val Cys Thr Cys Ser Leu Lys Asn Trp Arg Glu  
 420 425 430  
 Ala Leu Ala Leu Leu Thr Tyr Ser Gly Thr Glu Lys Phe Pro Glu  
 435 440 445  
 Leu Cys Asp Met Leu Gly Thr Arg Met Glu Gln Glu Gly Arg Arg Val  
 450 455 460  
 Leu Thr Ser Glu Ala Arg Leu Cys Tyr Val Cys Ser Gly Ser Val Glu  
 465 470 475 480  
 Arg Leu Val Glu Cys Trp Ala Lys Cys His Gln Ala Leu Ser Pro Met  
 485 490 495  
 Ala Leu Gln Asp Leu Met Glu Lys Val Met Val Leu Asn Arg Ser Leu  
 500 505 510  
 Glu Gln Leu Arg Gly Pro His Gly Val Ser Pro Gly Pro Ala Thr Thr  
 515 520 525  
 Tyr Arg Val Thr Gln Tyr Ala Asn Leu Leu Ala Ala Gln Gly Ser Leu  
 530 535 540  
 Ala Thr Ala Met Ser Phe Leu Pro Arg Asp Cys Ala Gln Pro Pro Val  
 545 550 555 560  
 Gln Gln Leu Arg Asp Arg Leu Phe His Ala Gln Gly Ser Ala Val Leu  
 565 570 575  
 Gly Gln Gln Ser Pro Pro Phe Pro Phe Pro Arg Ile Val Val Gly Ala  
 580 585 590  
 Thr Leu His Ser Lys Glu Thr Ser Ser Tyr Arg Leu Gly Ser Gln Pro  
 595 600 605  
 Ser His Gln Val Pro Thr Pro Ser Pro Arg Pro Arg Val Phe Thr Pro  
 610 615 620  
 Gln Ser Ser Pro Ala Met Pro Leu Ala Pro Ser His Pro Ser Pro Tyr  
 625 630 635 640  
 Gln Gly Pro Arg Thr Gln Asn Ile Ser Asp Tyr Arg Ala Pro Gly Pro  
 645 650 655  
 Gln Ala Ile Gln Pro Leu Pro Leu Ser Pro Gly Val Arg Pro Ala Ser  
 660 665 670  
 Ser Gln Pro Gln Leu Leu Gly Gly Gln Arg Val Gln Val Pro Asn Pro  
 675 680 685  
 Val Gly Phe Pro Gly Thr Trp Pro Leu Pro Gly Ser Pro Leu Pro Met  
 690 695 700  
 Ala Cys Pro Gly Ile Met Arg Pro Gly Ser Thr Ser Leu Pro Glu Thr  
 705 710 715 720  
 Pro Arg Leu Phe Pro Leu Leu Pro Leu Arg Pro Leu Gly Pro Gly Arg  
 725 730 735  
 Met Val Ser His Thr Pro Ala Pro Pro Ala Ser Phe Pro Val Pro Tyr  
 740 745 750  
 Leu Pro Gly Asp Pro Gly Ala Pro Cys Ser Ser Val Leu Pro Thr Thr  
 755 760 765  
 Gly Ile Leu Thr Pro His Pro Gly Pro Gln Asp Ser Trp Lys Glu Ala  
 770 775 780  
 Pro Ala Pro Arg Gly Asn Leu Gln Arg Asn Lys Leu Pro Glu Thr Phe  
 785 790 795 800  
 Met Pro Pro Ala Pro Ile Thr Ala Pro Val Met Ser Leu Thr Pro Glu  
 805 810 815  
 Leu Gln Gly Ile Leu Pro Ser Gln Pro Pro Val Ser Ser Val Ser His  
 820 825 830  
 Ala Pro Pro Gly Val Pro Gly Glu Leu Ser Leu Gln Leu Gln His Leu  
 835 840 845  
 Pro Pro Glu Lys Met Glu Arg Lys Glu Leu Pro Pro Glu His Gln Ser  
 850 855 860  
 Leu Lys Ser Ser Phe Glu Ala Leu Leu Gln Arg Cys Ser Leu Ser Ala  
 865 870 875 880  
 Thr Asp Leu Lys Thr Lys Arg Lys Leu Glu Glu Ala Ala Gln Arg Leu  
 885 890 895  
 Glu Tyr Leu Tyr Glu Lys Leu Cys Glu Gly Thr Leu Ser Pro His Val

900 905 910  
 Val Ala Gly Leu His Glu Val Ala Arg Cys Val Asp Ala Gly Ser Phe  
 915 920 925  
 Glu Gln Gly Leu Ala Val His Ala Gln Val Ala Gly Cys Ser Ser Phe  
 930 935 940  
 Ser Glu Val Ser Ser Phe Met Pro Ile Leu Lys Ala Val Leu Ile Ile  
 945 950 955 960  
 Ala His Lys Leu Leu Val \*  
 965 966

<210> 490  
 <211> 949  
 <212> PRT  
 <213> Homo sapiens

<400> 490  
 Met Val Phe Leu Pro Leu Lys Trp Ser Leu Ala Thr Met Ser Phe Leu  
 1 5 10 15  
 Leu Ser Ser Leu Leu Ala Leu Leu Thr Val Ser Thr Pro Ser Trp Cys  
 20 25 30  
 Gln Ser Thr Glu Ala Ser Pro Lys Arg Ser Asp Gly Thr Pro Phe Pro  
 35 40 45  
 Trp Asn Lys Ile Arg Leu Pro Glu Tyr Val Ile Pro Val His Tyr Asp  
 50 55 60  
 Leu Leu Ile His Ala Asn Leu Thr Thr Leu Thr Phe Trp Gly Thr Thr  
 65 70 75 80  
 Lys Val Glu Ile Thr Ala Ser Gln Pro Thr Ser Thr Ile Ile Leu His  
 85 90 95  
 Ser His His Leu Gln Ile Ser Arg Ala Thr Leu Arg Lys Gly Ala Gly  
 100 105 110  
 Glu Arg Leu Ser Glu Glu Pro Leu Gln Val Leu Glu His Pro Pro Gln  
 115 120 125  
 Glu Gln Ile Ala Leu Leu Ala Pro Glu Pro Leu Leu Val Gly Leu Pro  
 130 135 140  
 Tyr Thr Val Val Ile His Tyr Ala Gly Asn Leu Ser Glu Thr Phe His  
 145 150 155 160  
 Gly Phe Tyr Lys Ser Thr Tyr Arg Thr Lys Glu Gly Glu Leu Arg Ile  
 165 170 175  
 Leu Ala Ser Thr Gln Phe Glu Pro Thr Ala Ala Arg Met Ala Phe Pro  
 180 185 190  
 Cys Phe Asp Glu Pro Ala Phe Lys Ala Ser Phe Ser Ile Lys Ile Arg  
 195 200 205  
 Arg Glu Pro Arg His Leu Ala Ile Ser Asn Met Pro Leu Val Lys Ser  
 210 215 220  
 Val Thr Val Ala Glu Gly Leu Ile Glu Asp His Phe Asp Val Thr Val  
 225 230 235 240  
 Lys Met Ser Thr Tyr Leu Val Ala Phe Ile Ile Ser Asp Phe Glu Ser  
 245 250 255  
 Val Ser Lys Ile Thr Lys Ser Gly Val Lys Val Ser Val Tyr Ala Val  
 260 265 270  
 Pro Asp Lys Ile Asn Gln Ala Asp Tyr Ala Leu Asp Ala Ala Val Thr  
 275 280 285  
 Leu Leu Glu Phe Tyr Glu Asp Tyr Phe Ser Ile Pro Tyr Pro Leu Pro  
 290 295 300  
 Lys Gln Asp Leu Ala Ala Ile Pro Asp Phe Gln Ser Gly Ala Met Glu  
 305 310 315 320  
 Asn Trp Gly Leu Thr Thr Tyr Arg Glu Ser Ala Leu Leu Phe Asp Ala  
 325 330 335  
 Glu Lys Ser Ser Ala Ser Ser Lys Leu Gly Ile Thr Val Thr Val Ala  
 340 345 350  
 His Glu Leu Ala His Gln Trp Phe Gly Asn Leu Val Thr Met Glu Trp



355 360 365  
 Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala Lys Phe Met Glu Phe  
 370 375 380  
 Val Ser Val Ser Val Thr His Pro Glu Leu Lys Val Gly Asp Tyr Phe  
 385 390 395 400  
 Phe Gly Lys Cys Phe Asp Ala Met Glu Val Asp Ala Leu Asn Ser Ser  
 405 410 415  
 His Pro Val Ser Thr Pro Val Glu Asn Pro Ala Gln Ile Arg Glu Met  
 420 425 430  
 Phe Asp Asp Val Ser Tyr Asp Lys Gly Ala Cys Ile Leu Asn Met Leu  
 435 440 445  
 Arg Glu Tyr Leu Ser Ala Asp Ala Phe Lys Ser Gly Ile Val Gln Tyr  
 450 455 460  
 Leu Gln Lys His Ser Tyr Lys Asn Thr Lys Asn Glu Asp Leu Trp Asp  
 465 470 475 480  
 Ser Met Ala Ser Ile Cys Pro Thr Asp Gly Val Lys Gly Met Asp Gly  
 485 490 495  
 Phe Cys Ser Arg Ser Gln His Ser Ser Ser Ser His Trp His Gln  
 500 505 510  
 Glu Gly Val Asp Val Lys Thr Met Met Asn Thr Trp Thr Leu Gln Arg  
 515 520 525  
 Gly Phe Pro Leu Ile Thr Ile Thr Val Arg Gly Arg Asn Val His Met  
 530 535 540  
 Lys Gln Glu His Tyr Met Lys Gly Ser Asp Gly Ala Pro Asp Thr Gly  
 545 550 555 560  
 Tyr Leu Trp His Val Pro Leu Thr Phe Ile Thr Ser Lys Ser Asp Met  
 565 570 575  
 Val His Arg Phe Leu Leu Lys Thr Lys Thr Asp Val Leu Ile Leu Pro  
 580 585 590  
 Glu Glu Val Glu Trp Ile Lys Phe Asn Val Gly Met Asn Gly Tyr Tyr  
 595 600 605  
 Ile Val His Tyr Glu Asp Asp Gly Trp Asp Ser Leu Thr Gly Leu Leu  
 610 615 620  
 Lys Gly Thr His Thr Ala Val Ser Ser Asn Asp Arg Ala Ser Leu Ile  
 625 630 635 640  
 Asn Asn Ala Phe Gln Leu Val Ser Ile Gly Lys Leu Ser Ile Glu Lys  
 645 650 655  
 Ala Leu Asp Leu Ser Leu Tyr Leu Lys His Glu Thr Glu Ile Met Pro  
 660 665 670  
 Val Phe Gln Gly Leu Asn Glu Leu Ile Pro Met Tyr Lys Leu Met Glu  
 675 680 685  
 Lys Arg Asp Met Asn Glu Val Glu Thr Gln Phe Lys Ala Phe Leu Ile  
 690 695 700  
 Arg Leu Leu Arg Asp Leu Ile Asp Lys Gln Thr Trp Thr Asp Glu Gly  
 705 710 715 720  
 Ser Val Ser Glu Gln Met Leu Arg Ser Glu Leu Leu Leu Leu Ala Cys  
 725 730 735  
 Val His Asn Tyr Gln Pro Cys Val Gln Arg Ala Glu Gly Tyr Phe Arg  
 740 745 750  
 Lys Trp Lys Glu Ser Asn Gly Asn Leu Ser Leu Pro Val Asp Val Thr  
 755 760 765  
 Leu Ala Val Phe Ala Val Gly Ala Gln Ser Thr Glu Gly Trp Asp Phe  
 770 775 780  
 Leu Tyr Ser Lys Tyr Gln Phe Ser Leu Ser Ser Thr Glu Lys Ser Gln  
 785 790 795 800  
 Ile Glu Phe Ala Leu Cys Arg Thr Gln Asn Lys Glu Lys Leu Gln Trp  
 805 810 815  
 Leu Leu Asp Glu Ser Phe Lys Gly Asp Lys Ile Lys Thr Gln Glu Phe  
 820 825 830  
 Pro Gln Ile Leu Thr Leu Ile Gly Arg Asn Pro Val Gly Tyr Pro Leu  
 835 840 845  
 Ala Trp Gln Phe Leu Arg Lys Asn Trp Asn Lys Leu Val Gln Lys Phe  
 850 855 860

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Glu Leu Gly Ser Ser Ser Ile Ala His Met Val Met Gly Thr Thr Asn  
 865 870 875 880  
 Gln Phe Ser Thr Arg Thr Arg Leu Glu Glu Val Lys Gly Phe Phe Ser  
 885 890 895  
 Ser Leu Lys Glu Asn Gly Ser Gln Leu Arg Cys Val Gln Gln Thr Ile  
 900 905 910  
 Glu Thr Ile Glu Glu Asn Ile Gly Trp Met Asp Lys Asn Phe Asp Lys  
 915 920 925  
 Ile Arg Val Trp Leu Gln Ser Glu Lys Leu Glu His Asp Pro Glu Ala  
 930 935 940  
 Asp Ala Thr Gly \*  
 945 948

<210> 491  
 <211> 118  
 <212> PRT  
 <213> Homo sapiens

<400> 491  
 Met Lys Phe Gln Tyr Lys Glu Asp His Pro Phe Glu Tyr Arg Lys Lys  
 1 5 10 15  
 Glu Gly Glu Lys Ile Arg Lys Lys Tyr Pro Asp Arg Val Pro Val Ile  
 20 25 30  
 Val Glu Lys Ala Pro Lys Ala Arg Val Pro Asp Leu Asp Lys Arg Lys  
 35 40 45  
 Tyr Leu Val Pro Ser Asp Leu Thr Val Gly Gln Phe Tyr Phe Leu Ile  
 50 55 60  
 Arg Lys Arg Ile His Leu Arg Pro Glu Asp Ala Leu Phe Phe Phe Val  
 65 70 75 80  
 Asn Asn Thr Ile Pro Thr Ser Ala Thr Met Gly Gln Leu Tyr Glu  
 85 90 95  
 Asp Asn His Glu Glu Asp Tyr Phe Leu Tyr Val Ala Tyr Ser Asp Glu  
 100 105 110  
 Ser Val Tyr Gly Lys \*  
 115 117

<210> 492  
 <211> 503  
 <212> PRT  
 <213> Homo sapiens

<400> 492  
 Met Asp Arg Met Thr Glu Asp Ala Leu Arg Leu Asn Leu Leu Lys Arg  
 1 5 10 15  
 Ser Leu Asp Pro Ala Asp Glu Arg Asp Asp Val Leu Ala Lys Arg Leu  
 20 25 30  
 Lys Met Glu Gly His Glu Ala Met Glu Arg Leu Lys Met Leu Ala Leu  
 35 40 45  
 Leu Lys Arg Lys Asp Leu Ala Asn Leu Glu Val Pro His Glu Leu Pro  
 50 55 60  
 Thr Lys Gln Asp Gly Ser Gly Val Lys Gly Tyr Glu Glu Lys Leu Asn  
 65 70 75 80  
 Gly Asn Leu Arg Pro His Gly Asp Asn Arg Thr Ala Gly Arg Pro Gly  
 85 90 95  
 Lys Glu Asn Ile Asn Asp Glu Pro Val Asp Met Ser Ala Arg Arg Ser  
 100 105 110  
 Glu Pro Glu Arg Gly Arg Leu Thr Pro Ser Pro Asp Ile Ile Val Leu  
 115 120 125  
 Ser Asp Asn Glu Ala Ser Ser Pro Arg Ser Ser Ser Arg Met Glu Glu

130 135 140  
 Arg Leu Lys Ala Ala Asn Leu Glu Met Phe Lys Gly Lys Gly Ile Glu  
 145 150 155 160  
 Glu Arg Gln Gln Leu Ile Lys Gln Leu Arg Asp Glu Leu Arg Leu Glu  
 165 170 175  
 Glu Ala Arg Leu Val Leu Leu Lys Lys Leu Arg Gln Ser Gln Leu Gln  
 180 185 190  
 Lys Glu Asn Val Val Gln Lys Thr Pro Val Val Gln Asn Ala Ala Ser  
 195 200 205  
 Ile Val Gln Pro Ser Pro Ala His Val Gly Gln Gln Gly Leu Ser Lys  
 210 215 220  
 Leu Pro Ser Arg Pro Gly Ala Gln Gly Val Glu Pro Gln Asn Leu Arg  
 225 230 235 240  
 Thr Leu Gln Gly His Ser Val Ile Arg Ser Ala Thr Asn Thr Thr Leu  
 245 250 255  
 Pro His Met Leu Met Ser Gln Arg Val Ile Ala Pro Asn Pro Ala Gln  
 260 265 270  
 Leu Gln Gly Gln Arg Gly Pro Pro Lys Pro Gly Leu Val Arg Thr Thr  
 275 280 285  
 Thr Pro Asn Met Asn Pro Ala Ile Asn Tyr Gln Pro Gln Ser Ser Ser  
 290 295 300  
 Ser Val Pro Cys Gln Arg Thr Thr Ser Ser Ala Ile Tyr Met Asn Leu  
 305 310 315 320  
 Ala Ser His Ile Gln Pro Gly Thr Val Asn Arg Val Ser Ser Pro Leu  
 325 330 335  
 Pro Ser Pro Ser Ala Met Thr Asp Ala Ala Asn Ser Gln Ala Ala Ala  
 340 345 350  
 Lys Leu Ala Leu Arg Lys Gln Leu Glu Lys Thr Leu Leu Glu Ile Pro  
 355 360 365  
 Pro Pro Lys Pro Pro Ala Pro Leu Leu His Phe Leu Pro Ser Ala Ala  
 370 375 380  
 Asn Ser Glu Phe Ile Tyr Met Val Gly Leu Glu Glu Val Val Gln Ser  
 385 390 395 400  
 Val Ile Asp Ser Gln Gly Lys Ser Cys Ala Ser Leu Leu Arg Val Glu  
 405 410 415  
 Pro Phe Val Cys Ala Gln Cys Arg Thr Asp Phe Thr Pro His Trp Lys  
 420 425 430  
 Gln Glu Lys Asn Gly Lys Ile Leu Cys Glu Gln Cys Met Thr Ser Asn  
 435 440 445  
 Gln Lys Lys Ala Leu Lys Ala Glu His Thr Asn Arg Leu Lys Asn Ala  
 450 455 460  
 Phe Val Lys Ala Leu Gln Gln Glu Gln Val Arg Ile Leu Thr Ala His  
 465 470 475 480  
 Trp Pro Pro Val Pro Val Cys Phe Phe Gln Arg Val Ala Pro Ser Ser  
 485 490 495  
 Leu Gln Glu Trp Phe Met \*  
 500 502

<210> 493  
 <211> 112  
 <212> PRT  
 <213> Homo sapiens

<400> 493  
 Met Trp Lys Gly Arg Ser His Pro Phe Leu Pro Cys Ser Ser Arg  
 1 5 10 15  
 Arg Ala Gly Ser Gly Gly Gln Leu Asp Ser Ile Leu Pro His Gln Ser  
 20 25 30  
 Pro Ala Trp Gly Pro Trp Gly Cys Lys Asp Leu Ser Ser Gly Val Pro  
 35 40 45  
 Ser Phe Leu Thr Ser Ser Ile Leu Trp Lys Ser Ala Val Phe Ala Glu

```

      50              55              60
Asp Asn Gly Leu Lys Ile His Pro Cys Ser Cys Lys Arg His Asp Leu
65              70              75              80
Ala Val Phe Tyr Gly Cys Thr Ser Phe Val Leu Thr Phe Gly Leu Ser
      85              90              95
Pro Trp Phe Leu Thr Gln Ser Phe Leu Asn Pro Leu Glu Phe Ser Gly
      100              105              110              112

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<210> 494  
 <211> 279  
 <212> PRT  
 <213> Homo sapiens

```

      <400> 494
Met Pro Asp Gln Ala Leu Gln Gln Met Leu Asp Arg Ser Cys Trp Val
1              5              10              15
Cys Phe Ala Thr Asp Glu Asp Asp Arg Thr Ala Glu Trp Val Arg Pro
      20              25              30
Cys Arg Cys Arg Gly Ser Thr Lys Trp Val His Gln Ala Cys Leu Gln
      35              40              45
Arg Trp Val Asp Glu Lys Gln Arg Gly Asn Ser Thr Ala Arg Val Ala
      50              55              60
Cys Pro Gln Cys Asn Ala Glu Tyr Leu Ile Val Phe Pro Lys Leu Gly
65              70              75              80
Pro Val Val Tyr Val Leu Asp Leu Ala Asp Arg Leu Ile Ser Lys Ala
      85              90              95
Cys Pro Phe Ala Ala Ala Gly Ile Met Val Gly Ser Ile Tyr Trp Thr
      100              105              110
Ala Val Thr Tyr Gly Ala Val Thr Val Met Gln Val Val Gly His Lys
      115              120              125
Glu Gly Leu Asp Val Met Glu Arg Ala Asp Pro Leu Phe Leu Leu Ile
130              135              140
Gly Leu Pro Thr Ile Pro Val Met Leu Ile Leu Gly Lys Met Ile Arg
145              150              155              160
Trp Glu Asp Tyr Val Leu Arg Leu Trp Arg Lys Tyr Ser Asn Lys Leu
      165              170              175
Gln Ile Leu Asn Ser Ile Phe Pro Gly Ile Gly Cys Pro Val Pro Arg
      180              185              190
Ile Pro Ala Glu Ala Asn Pro Leu Ala Asp His Val Ser Ala Thr Arg
      195              200              205
Ile Leu Cys Gly Ala Leu Val Phe Pro Thr Ile Ala Thr Ile Val Gly
210              215              220
Lys Leu Met Phe Ser Ser Val Asn Ser Asn Leu Gln Arg Thr Ile Leu
225              230              235              240
Gly Gly Ile Ala Phe Val Ala Ile Lys Gly Ala Phe Lys Val Tyr Phe
      245              250              255
Lys Gln Gln Gln Tyr Leu Arg Gln Ala His Arg Lys Ile Leu Asn Tyr
      260              265              270
Pro Glu Gln Glu Glu Ala *
      275              278

```

<210> 495  
 <211> 936  
 <212> PRT  
 <213> Homo sapiens

<400> 495

Met Arg Asp Leu Glu Leu Arg Glu Val Lys Gln Leu Ala Arg Gly His  
 1 5 10 15  
 Thr Ala Gly Tyr Lys Thr Leu Leu Lys Cys Leu Ser Gly Lys Phe Cys  
 20 25 30  
 Arg Arg Glu Leu Ile Gly Ile Met Gly Pro Ser Gly Ala Gly Lys Ser  
 35 40 45  
 Thr Phe Met Asn Ile Leu Ala Gly Tyr Arg Glu Ser Gly Met Lys Gly  
 50 55 60  
 Gln Ile Leu Val Asn Gly Arg Pro Arg Glu Leu Arg Thr Phe Arg Lys  
 65 70 75 80  
 Met Ser Cys Tyr Ile Met Gln Asp Asp Met Leu Leu Pro His Leu Thr  
 85 90 95  
 Val Leu Glu Ala Met Met Val Ser Ala Asn Leu Lys Leu Ser Glu Lys  
 100 105 110  
 Gln Glu Val Lys Lys Glu Leu Val Thr Glu Ile Leu Thr Ala Leu Gly  
 115 120 125  
 Leu Met Ser Cys Ser His Thr Arg Thr Ala Leu Leu Ser Gly Gly Gln  
 130 135 140  
 Arg Lys Arg Leu Ala Ile Ala Leu Glu Leu Val Asn Asn Pro Pro Val  
 145 150 155 160  
 Met Phe Phe Asp Glu Pro Thr Ser Gly Leu Asp Ser Ala Ser Cys Phe  
 165 170 175  
 Gln Val Val Ser Leu Met Lys Ser Leu Ala Gln Gly Gly Arg Thr Ile  
 180 185 190  
 Ile Cys Thr Ile His Gln Pro Ser Ala Lys Leu Phe Glu Met Phe Asp  
 195 200 205  
 Lys Cys Ile Phe Lys Gly Val Val Thr Asn Leu Ile Pro Tyr Leu Lys  
 210 215 220  
 Gly Leu Gly Leu His Cys Pro Thr Tyr His Asn Pro Ala Asp Phe Ile  
 225 230 235 240  
 Ile Glu Val Ala Ser Gly Glu Tyr Gly Asp Leu Asn Pro Met Leu Phe  
 245 250 255  
 Arg Ala Val Gln Asn Gly Leu Cys Ala Met Ala Glu Lys Lys Ser Ser  
 260 265 270  
 Pro Glu Lys Asn Glu Val Pro Ala Pro Cys Pro Pro Cys Pro Pro Glu  
 275 280 285  
 Val Asp Pro Ile Glu Ser His Thr Phe Ala Thr Ser Thr Leu Thr Gln  
 290 295 300  
 Phe Cys Ile Leu Phe Lys Arg Thr Phe Leu Ser Ile Leu Arg Asp Thr  
 305 310 315 320  
 Val Val Cys Pro Val Val Tyr Cys Ser Ile Val Tyr Trp Met Thr Gly  
 325 330 335  
 Gln Pro Ala Glu Thr Ser Arg Phe Leu Leu Phe Ser Ala Leu Ala Thr  
 340 345 350  
 Ala Thr Ala Leu Val Ala Gln Ser Leu Gly Leu Leu Ile Gly Ala Ala  
 355 360 365  
 Ser Asn Ser Leu Gln Val Ala Thr Phe Val Gly Pro Val Thr Ala Ile  
 370 375 380  
 Pro Val Leu Leu Phe Ser Gly Phe Phe Val Ser Phe Lys Thr Ile Pro  
 385 390 395 400  
 Thr Tyr Leu Gln Trp Ser Ser Tyr Leu Ser Tyr Val Arg Tyr Gly Phe  
 405 410 415  
 Glu Gly Val Ile Leu Thr Ile Tyr Gly Met Glu Arg Gly Asp Leu Thr  
 420 425 430  
 Cys Leu Glu Glu Arg Cys Pro Phe Arg Glu Pro Gln Ser Ile Leu Arg  
 435 440 445  
 Ala Leu Asp Val Glu Asp Ala Lys Leu Tyr Met Asp Phe Leu Val Leu  
 450 455 460  
 Gly Ile Phe Phe Leu Ala Leu Arg Leu Leu Ala Tyr Leu Val Leu Arg  
 465 470 475 480  
 Tyr Arg Glu Cys Gly Phe Cys Ser Leu Asp Ser Ser Ala Asp Leu Ile  
 485 490 495  
 Arg His Val Tyr Phe His Cys Tyr His Thr Lys Leu Lys Gln Trp Gly

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      500      505      510
Leu Gln Ala Leu Gln Ser Gln Ala Asp Leu Gly Pro Cys Ile Leu Asp
      515      520      525
Phe Gln Ser Arg Asn Val Ile Pro Asp Ile Pro Asp His Phe Leu Cys
      530      535      540
Leu Trp Glu His Cys Glu Leu Pro Leu Ala Gln Asn Ser Phe Asp Asn
545      550      555      560
Pro Glu Trp Phe Tyr Arg His Val Glu Ala His Ser Leu Cys Cys Glu
      565      570      575
Tyr Glu Ala Val Gly Lys Asp Asn Pro Val Val Leu Cys Gly Trp Lys
      580      585      590
Gly Cys Thr Cys Thr Phe Lys Asp Arg Ser Lys Leu Arg Glu His Leu
      595      600      605
Arg Ser His Thr Gln Glu Lys Val Val Ala Cys Pro Thr Cys Gly Gly
      610      615      620
Met Phe Ala Asn Asn Thr Lys Phe Leu Asp His Ile Arg Arg Gln Thr
625      630      635      640
Ser Leu Asp Gln Gln His Phe Gln Cys Ser His Cys Ser Lys Arg Phe
      645      650      655
Ala Thr Glu Arg Leu Leu Arg Asp His Met Arg Asn His Val Asn His
      660      665      670
Tyr Lys Cys Pro Leu Cys Asp Met Thr Cys Pro Leu Pro Ser Ser Leu
675      680      685
Arg Asn His Met Arg Phe Arg His Ser Glu Asp Arg Pro Phe Lys Cys
      690      695      700
Asp Cys Cys Asp Tyr Ser Cys Lys Asn Leu Ile Asp Leu Gln Lys His
705      710      715      720
Leu Asp Thr His Ser Glu Glu Pro Ala Tyr Arg Cys Asp Phe Glu Asn
      725      730      735
Cys Thr Phe Ser Ala Arg Ser Leu Cys Ser Ile Lys Ser His Tyr Arg
      740      745      750
Lys Val His Glu Gly Asp Ser Glu Pro Arg Tyr Lys Cys His Val Cys
      755      760      765
Asp Lys Cys Phe Thr Arg Gly Asn Asn Leu Thr Val His Leu Arg Lys
      770      775      780
Lys His Gln Phe Lys Trp Pro Ser Gly His Pro Arg Phe Arg Tyr Lys
785      790      795      800
Glu His Glu Asp Gly Tyr Met Arg Leu Gln Leu Val Arg Tyr Glu Ser
      805      810      815
Val Glu Leu Thr Gln Gln Leu Leu Arg Gln Pro Gln Glu Gly Ser Gly
      820      825      830
Leu Gly Thr Ser Leu Asn Glu Ser Ser Leu Gln Gly Ile Ile Leu Glu
      835      840      845
Thr Val Pro Gly Glu Pro Gly Arg Lys Glu Glu Glu Glu Glu Gly Lys
      850      855      860
Gly Ser Glu Gly Thr Ala Leu Ser Ala Ser Gln Asp Asn Pro Ser Ser
865      870      875      880
Val Ile His Val Val Asn Gln Thr Asn Ala Gln Gly Gln Gln Glu Ile
      885      890      895
Val Tyr Tyr Val Leu Ser Glu Ala Pro Gly Glu Pro Pro Pro Val Pro
      900      905      910
Glu Pro Pro Ser Gly Gly Ile Met Glu Lys Leu Gln Gly Ile Ala Glu
      915      920      925
Glu Pro Glu Ile Gln Met Val *
      930      935

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&lt;210&gt; 496

&lt;211&gt; 150

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 496

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Met Glu Ala Asn His Cys Ser Leu Gly Val Tyr Pro Ser Tyr Pro Asp
 1          5          10          15
Leu Val Ile Asp Val Gly Glu Val Thr Leu Gly Glu Glu Asn Arg Lys
          20          25          30
Lys Leu Gln Lys Thr Gln Arg Asp Gln Glu Arg Ala Arg Val Ile Arg
          35          40          45
Ala Ala Cys Ala Leu Leu Asn Ser Gly Gly Gly Val Ile Gln Met Glu
          50          55          60
Met Ala Asn Arg Asp Glu Arg Pro Thr Glu Met Gly Leu Asp Leu Glu
          65          70          75          80
Glu Ser Leu Arg Lys Leu Ile Gln Tyr Pro Tyr Leu Gln Ala Phe Phe
          85          90          95
Glu Thr Lys Gln His Gly Arg Cys Phe Tyr Ile Phe Val Lys Ser Trp
          100          105          110
Ser Gly Asp Pro Phe Leu Lys Asp Gly Ser Phe Asn Ser Arg Ile Cys
          115          120          125
Ser Leu Thr Ser Ala Ile Tyr Met Gln Met Asn Glu Thr Arg Pro Leu
          130          135          140
Phe His Thr Ile Tyr *
145          149

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&lt;210&gt; 497

&lt;211&gt; 1140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 497

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Met Arg Leu Glu Glu Gln Lys Lys Lys Leu Ala Phe Leu Leu Lys Asp
 1          5          10          15
Trp Glu Lys Cys Glu Lys Gly Ile Ala Asp Ser Leu Glu Lys Leu Arg
          20          25          30
Thr Phe Lys Lys Lys Leu Ser Gln Ser Leu Pro Asp His His Glu Glu
          35          40          45
Leu His Ala Glu Gln Met Arg Cys Lys Glu Leu Glu Asn Ala Val Gly
          50          55          60
Ser Trp Thr Asp Asp Leu Thr Gln Leu Ser Leu Leu Lys Asp Thr Leu
          65          70          75          80
Ser Ala Tyr Ile Ser Ala Asp Asp Ile Ser Ile Leu Asn Glu Arg Val
          85          90          95
Glu Leu Leu Gln Arg Gln Trp Glu Glu Lys Cys His Gln Leu Ser Leu
          100          105          110
Arg Arg Gln Gln Ile Gly Glu Arg Leu Asn Glu Trp Ala Val Phe Ser
          115          120          125
Glu Lys Asn Lys Glu Leu Cys Glu Trp Leu Thr Gln Met Glu Ser Lys
          130          135          140
Val Ser Gln Asn Gly Asp Ile Leu Ile Glu Glu Met Ile Glu Lys Leu
          145          150          155          160
Lys Lys Asp Tyr Gln Glu Glu Ile Ala Ile Ala Gln Glu Asn Lys Ile
          165          170          175
Gln Leu Gln Gln Met Gly Glu Arg Leu Ala Lys Ala Ser His Glu Ser
          180          185          190
Lys Ala Ser Glu Ile Glu Tyr Lys Leu Gly Lys Val Asn Asp Arg Trp
          195          200          205
Gln His Leu Leu Asp Leu Ile Ala Ala Arg Val Lys Lys Leu Lys Glu
          210          215          220
Thr Leu Val Ala Val Gln Gln Leu Asp Lys Asn Met Ser Ser Leu Arg
          225          230          235          240
Thr Trp Leu Ala His Ile Glu Ser Glu Leu Ala Lys Pro Ile Val Tyr
          245          250          255
Asp Ser Cys Asn Ser Glu Glu Ile Gln Arg Lys Leu Asn Glu Gln Gln

```

260 265 270  
 Glu Leu Gln Arg Asp Ile Glu Lys His Ser Thr Gly Val Ala Ser Val  
 275 280 285  
 Leu Asn Leu Cys Glu Val Leu Leu His Asp Cys Asp Ala Cys Ala Thr  
 290 295 300  
 Asp Ala Glu Cys Asp Ser Ile Gln Gln Ala Thr Arg Asn Leu Asp Arg  
 305 310 315 320  
 Arg Trp Arg Asn Ile Cys Ala Met Ser Met Glu Arg Arg Leu Lys Ile  
 325 330 335  
 Glu Glu Thr Trp Arg Leu Trp Gln Lys Phe Leu Asp Asp Tyr Ser Arg  
 340 345 350  
 Phe Glu Asp Trp Leu Lys Ser Ser Glu Arg Thr Ala Ala Phe Pro Ser  
 355 360 365  
 Ser Ser Gly Val Ile Tyr Thr Val Ala Lys Glu Glu Leu Lys Lys Phe  
 370 375 380  
 Glu Ala Phe Gln Arg Gln Val His Glu Cys Leu Thr Gln Leu Glu Leu  
 385 390 395 400  
 Ile Asn Lys Gln Tyr Arg Arg Leu Ala Arg Glu Asn Arg Thr Asp Ser  
 405 410 415  
 Ala Cys Ser Leu Lys Gln Met Val His Glu Gly Asn Gln Arg Trp Asp  
 420 425 430  
 Asn Leu Gln Lys Arg Val Thr Ser Ile Leu Arg Arg Leu Lys His Phe  
 435 440 445  
 Ile Gly Gln Arg Glu Glu Phe Glu Thr Ala Arg Asp Ser Ile Leu Val  
 450 455 460  
 Trp Leu Thr Glu Met Asp Leu Gln Leu Thr Asn Ile Glu His Phe Ser  
 465 470 475 480  
 Glu Cys Asp Val Gln Ala Lys Ile Lys Gln Leu Lys Ala Phe Gln Gln  
 485 490 495  
 Glu Ile Ser Leu Asn His Asn Lys Ile Glu Gln Ile Ile Ala Gln Gly  
 500 505 510  
 Glu Gln Leu Ile Glu Lys Ser Glu Pro Leu Asp Ala Ala Ile Ile Glu  
 515 520 525  
 Glu Glu Leu Asp Glu Leu Arg Arg Tyr Cys Gln Glu Ala Phe Gly Arg  
 530 535 540  
 Val Glu Arg Tyr His Lys Lys Leu Ile Arg Leu Pro Leu Pro Asp Asp  
 545 550 555 560  
 Glu His Asp Leu Ser Asp Arg Glu Leu Glu Leu Glu Asp Ser Ala Ala  
 565 570 575  
 Leu Ser Asp Leu His Trp His Asp Arg Ser Ala Asp Ser Leu Leu Ser  
 580 585 590  
 Pro Gln Pro Ser Ser Asn Leu Ser Leu Ser Leu Ala Gln Pro Leu Arg  
 595 600 605  
 Ser Glu Arg Ser Gly Arg Asp Thr Pro Ala Ser Val Asp Ser Ile Pro  
 610 615 620  
 Leu Glu Trp Asp His Asp Tyr Asp Leu Ser Arg Asp Leu Glu Ser Ala  
 625 630 635 640  
 Met Ser Arg Ala Leu Pro Ser Glu Asp Glu Glu Gly Gln Asp Asp Lys  
 645 650 655  
 Asp Phe Tyr Leu Arg Gly Ala Val Gly Leu Ser Gly Asp His Ser Ala  
 660 665 670  
 Leu Glu Ser Gln Ile Arg Gln Leu Gly Lys Ala Leu Asp Asp Ser Arg  
 675 680 685  
 Phe Gln Ile Gln Gln Thr Glu Asn Ile Ile Arg Ser Lys Thr Pro Thr  
 690 695 700  
 Gly Pro Glu Leu Asp Thr Ser Tyr Lys Gly Tyr Met Lys Leu Leu Gly  
 705 710 715 720  
 Glu Cys Ser Ser Ser Ile Asp Ser Val Lys Arg Leu Glu His Lys Leu  
 725 730 735  
 Lys Glu Glu Glu Glu Ser Leu Pro Gly Phe Val Asn Leu His Ser Thr  
 740 745 750  
 Glu Thr Gln Thr Ala Gly Val Ile Asp Arg Trp Glu Leu Leu Gln Ala  
 755 760 765



Gln Ala Leu Ser Lys Glu Leu Arg Met Lys Gln Asn Leu Gln Lys Trp  
 770 775 780  
 Gln Gln Phe Asn Ser Asp Leu Asn Ser Ile Trp Ala Trp Leu Gly Asp  
 785 790 795 800  
 Thr Glu Glu Glu Leu Glu Gln Leu Gln Arg Leu Glu Leu Ser Thr Asp  
 805 810 815  
 Ile Gln Thr Ile Glu Leu Gln Ile Lys Lys Leu Lys Glu Leu Gln Lys  
 820 825 830  
 Ala Val Asp His Arg Lys Ala Ile Ile Leu Ser Ile Asn Leu Cys Ser  
 835 840 845  
 Pro Glu Phe Thr Gln Ala Asp Ser Lys Glu Ser Arg Asp Leu Gln Asp  
 850 855 860  
 Arg Leu Ser Gln Met Asn Gly Arg Trp Asp Arg Val Cys Ser Leu Leu  
 865 870 875 880  
 Glu Glu Trp Arg Gly Leu Leu Gln Asp Ala Leu Met Gln Cys Gln Gly  
 885 890 895  
 Phe His Glu Met Ser His Gly Leu Leu Leu Met Leu Glu Asn Ile Asp  
 900 905 910  
 Arg Arg Lys Asn Glu Ile Val Pro Ile Asp Ser Asn Leu Asp Ala Glu  
 915 920 925  
 Ile Leu Gln Asp His His Lys Gln Leu Met Gln Ile Lys His Glu Leu  
 930 935 940  
 Leu Glu Ser Gln Leu Arg Val Ala Ser Leu Gln Asp Met Ser Cys Gln  
 945 950 955 960  
 Leu Leu Val Asn Ala Glu Gly Thr Asp Cys Leu Glu Ala Lys Glu Lys  
 965 970 975  
 Val His Val Ile Gly Asn Arg Leu Lys Leu Leu Leu Lys Glu Val Ser  
 980 985 990  
 Arg His Ile Lys Glu Leu Glu Lys Leu Leu Asp Val Ser Ser Ser Gln  
 995 1000 1005  
 Gln Asp Leu Ser Ser Trp Ser Ser Ala Asp Glu Leu Asp Thr Ser Gly  
 1010 1015 1020  
 Ser Val Ser Pro Thr Ser Gly Arg Ser Thr Pro Asn Arg Gln Lys Thr  
 1025 1030 1035 1040  
 Pro Arg Gly Lys Cys Ser Leu Ser Gln Pro Gly Pro Ser Val Ser Ser  
 1045 1050 1055  
 Pro His Ser Arg Ser Thr Lys Gly Gly Ser Asp Ser Ser Leu Ser Glu  
 1060 1065 1070  
 Pro Gly Pro Gly Arg Ser Gly Arg Gly Phe Met Phe Arg Val Leu Arg  
 1075 1080 1085  
 Ala Ala Leu Pro Leu Gln Leu Leu Leu Leu Leu Ile Gly Leu Ala  
 1090 1095 1100  
 Cys Leu Val Pro Met Ser Glu Glu Asp Tyr Ser Cys Ala Leu Ser Asn  
 1105 1110 1115 1120  
 Asn Phe Ala Arg Ser Phe His Pro Met Leu Arg Tyr Thr Asn Gly Pro  
 1125 1130 1135  
 Pro Pro Leu \*  
 1139

<210> 498  
 <211> 1154  
 <212> PRT  
 <213> Homo sapiens

<400> 498  
 Met Arg Leu Glu Glu Gln Lys Lys Lys Leu Ala Phe Leu Leu Lys Asp  
 1 5 10 15  
 Trp Glu Lys Cys Glu Lys Gly Ile Ala Asp Ser Leu Glu Lys Leu Arg  
 20 25 30  
 Thr Phe Lys Lys Lys Leu Ser Gln Ser Leu Pro Asp His His Glu Glu  
 35 40 45

Leu His Ala Glu Gln Met Arg Cys Lys Glu Leu Glu Asn Ala Val Gly  
 50 55 60  
 Ser Trp Thr Asp Asp Leu Thr Gln Leu Ser Leu Leu Lys Asp Thr Leu  
 65 70 75 80  
 Ser Ala Tyr Ile Ser Ala Asp Asp Ile Ser Ile Leu Asn Glu Arg Val  
 85 90 95  
 Glu Leu Leu Gln Arg Gln Trp Glu Glu Leu Cys His Gln Leu Ser Leu  
 100 105 110  
 Arg Arg Gln Gln Ile Gly Glu Arg Leu Asn Glu Trp Ala Val Phe Ser  
 115 120 125  
 Glu Lys Asn Lys Glu Leu Cys Glu Trp Leu Thr Gln Met Glu Ser Lys  
 130 135 140  
 Val Ser Gln Asn Gly Asp Ile Leu Ile Glu Glu Met Ile Glu Lys Leu  
 145 150 155 160  
 Lys Lys Asp Tyr Gln Glu Glu Ile Ala Ile Ala Gln Glu Asn Lys Ile  
 165 170 175  
 Gln Leu Gln Gln Met Gly Glu Arg Leu Ala Lys Ala Ser His Glu Ser  
 180 185 190  
 Lys Ala Ser Glu Ile Glu Tyr Lys Leu Gly Lys Val Asn Asp Arg Trp  
 195 200 205  
 Gln His Leu Leu Asp Leu Ile Ala Ala Arg Val Lys Lys Leu Lys Glu  
 210 215 220  
 Thr Leu Val Ala Val Gln Gln Leu Asp Lys Asn Met Ser Ser Leu Arg  
 225 230 235 240  
 Thr Trp Leu Ala His Ile Glu Ser Glu Leu Ala Lys Pro Ile Val Tyr  
 245 250 255  
 Asp Ser Cys Asn Ser Glu Glu Ile Gln Arg Lys Leu Asn Glu Gln Gln  
 260 265 270  
 Glu Leu Gln Arg Asp Ile Glu Lys His Ser Thr Gly Val Ala Ser Val  
 275 280 285  
 Leu Asn Leu Cys Glu Val Leu Leu His Asp Cys Asp Ala Cys Ala Thr  
 290 295 300  
 Asp Ala Glu Cys Asp Ser Ile Gln Gln Ala Thr Arg Asn Leu Asp Arg  
 305 310 315 320  
 Arg Trp Arg Asn Ile Cys Ala Met Ser Met Glu Arg Arg Leu Lys Ile  
 325 330 335  
 Glu Glu Thr Trp Arg Leu Trp Gln Lys Phe Leu Asp Asp Tyr Ser Arg  
 340 345 350  
 Phe Glu Asp Trp Leu Lys Ser Ser Glu Arg Thr Ala Ala Phe Pro Ser  
 355 360 365  
 Ser Ser Gly Val Ile Tyr Thr Val Ala Lys Glu Glu Leu Lys Lys Phe  
 370 375 380  
 Glu Ala Phe Gln Arg Gln Val His Glu Cys Leu Thr Gln Leu Glu Leu  
 385 390 395 400  
 Ile Asn Lys Gln Tyr Arg Arg Leu Ala Arg Glu Asn Arg Thr Asp Ser  
 405 410 415  
 Ala Cys Ser Leu Lys Gln Met Val His Glu Gly Asn Gln Arg Trp Asp  
 420 425 430  
 Asn Leu Gln Lys Arg Val Thr Ser Ile Leu Arg Arg Leu Lys His Phe  
 435 440 445  
 Ile Gly Gln Arg Glu Glu Phe Glu Thr Ala Arg Asp Ser Ile Leu Val  
 450 455 460  
 Trp Leu Thr Glu Met Asp Leu Gln Leu Thr Asn Ile Glu His Phe Ser  
 465 470 475 480  
 Glu Cys Asp Val Gln Ala Lys Ile Lys Gln Leu Lys Ala Phe Gln Gln  
 485 490 495  
 Glu Ile Ser Leu Asn His Asn Lys Ile Glu Gln Ile Ile Ala Gln Gly  
 500 505 510  
 Glu Gln Leu Ile Glu Lys Ser Glu Pro Leu Asp Ala Ala Ile Ile Glu  
 515 520 525  
 Glu Glu Leu Asp Glu Leu Arg Arg Tyr Cys Gln Glu Ala Phe Gly Arg  
 530 535 540  
 Val Glu Arg Tyr His Lys Lys Leu Ile Arg Leu Pro Leu Pro Asp Asp

**PCT/US00/34960**

446

Gly Lys Cys Ser Leu Ser Gln Pro Gly Pro Ser Val Ser Ser Pro His  
                   1060                  1065                  1070  
 Ser Arg Ser Thr Lys Gly Gly Ser Asp Ser Ser Leu Ser Glu Pro Gly  
                   1075                  1080                  1085  
 Pro Gly Arg Ser Gly Arg Gly Phe Met Phe Arg Val Leu Arg Ala Ala  
                   1090                  1095                  1100  
 Leu Pro Leu Gln Leu Leu Leu Leu Leu Ile Gly Leu Ala Cys Leu  
 1105                  1110                  1115                  1120  
 Val Pro Met Ser Glu Glu Asp Tyr Ser Cys Ala Leu Ser Asn Asn Phe  
                   1125                  1130                  1135  
 Ala Arg Ser Phe His Pro Met Leu Arg Tyr Thr Asn Gly Pro Pro Pro  
                   1140                  1145                  1150  
 Leu \*  
 1153

<210> 499  
 <211> 303  
 <212> PRT  
 <213> Homo sapiens

<400> 499  
 Met Asp Tyr Lys Ser Ser Leu Ile Gln Asp Gly Asn Pro Met Glu Asn  
   1                  5                  10                  15  
 Leu Glu Lys Gln Leu Ile Cys Pro Ile Cys Leu Glu Met Phe Thr Lys  
                   20                  25                  30  
 Pro Val Val Ile Leu Pro Cys Gln His Asn Leu Cys Arg Lys Cys Ala  
                   35                  40                  45  
 Asn Asp Ile Phe Gln Ala Ala Asn Pro Tyr Trp Thr Ser Arg Gly Ser  
                   50                  55                  60  
 Ser Val Ser Met Ser Gly Arg Phe Arg Cys Pro Thr Cys Arg His  
                   65                  70                  75                  80  
 Glu Val Ile Met Asp Arg His Gly Val Tyr Gly Leu Gln Arg Asn Leu  
                   85                  90                  95  
 Leu Val Glu Asn Ile Ile Asp Ile Tyr Lys Gln Glu Cys Ser Ser Arg  
                   100                  105                  110  
 Pro Leu Gln Lys Gly Ser His Pro Met Cys Lys Glu His Glu Asp Glu  
                   115                  120                  125  
 Lys Ile Asn Ile Tyr Cys Leu Thr Cys Glu Val Pro Thr Cys Ser Met  
                   130                  135                  140  
 Cys Lys Val Phe Gly Ile His Lys Ala Cys Glu Val Ala Pro Leu Gln  
                   145                  150                  155                  160  
 Ser Val Phe Gln Gly Gln Lys Thr Glu Leu Asn Asn Cys Ile Ser Met  
                   165                  170                  175  
 Leu Val Ala Gly Asn Asp Arg Val Gln Thr Ile Ile Thr Gln Leu Glu  
                   180                  185                  190  
 Asp Ser Arg Arg Val Thr Lys Glu Asn Ser His Gln Val Lys Glu Glu  
                   195                  200                  205  
 Leu Ser Gln Lys Phe Asp Thr Leu Tyr Ala Ile Leu Asp Glu Lys Lys  
                   210                  215                  220  
 Ser Glu Leu Leu Gln Arg Ile Thr Gln Glu Gln Glu Lys Lys Leu Ser  
                   225                  230                  235                  240  
 Phe Ile Glu Ala Leu Ile Gln Gln Tyr Gln Glu Gln Leu Asp Lys Ser  
                   245                  250                  255  
 Thr Lys Leu Val Glu Thr Ala Ile Gln Ser Leu Asp Glu Pro Gly Gly  
                   260                  265                  270  
 Ala Thr Phe Leu Leu Val Ser Arg Thr Arg Arg Val Trp Val Gly Ser  
                   275                  280                  285  
 Val Gln Leu Tyr Ser Ser Lys Val Gln Val Met Leu Pro His \*  
                   290                  295                  300                  302

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<212> PRT  
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Pro Pro Val Lys Glu Ala Ala Glu Ser Gly Ile Ile Lys Val Lys Thr  
35 40 45  
Ile Ala Ala Arg Asn Thr Glu Ile Leu Ala Ala Leu Lys Glu Asn Ser  
50 55 60  
Ser Glu Val Val Gln Pro Phe Leu Met Gly Cys Gly Thr Lys Glu Pro  
65 70 75 80  
Lys Ile Thr Gln Leu Cys Leu Ala Ala Ile Gln Arg Leu Met Ser His  
85 90 95  
Glu Val Val Ser Glu Thr Ala Ala Gly Asn Ile Ile Asn Met Leu Trp  
100 105 110  
Gln Leu Met Glu Asn Ser Leu Glu Glu Leu Lys Leu Leu Gln Thr Val  
115 120 125  
Leu Val Leu Leu Thr Thr Asn Thr Val Val His Asp Glu Ala Leu Ser  
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Lys Val Gly Lys Leu Phe Ala Arg Val His Met Cys Phe Glu Thr Val  
145 150 155 160  
Phe Glu \*  
162

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20 25 30  
Thr Phe Leu Thr Arg Arg Asn Ile Val Gly Cys Arg Ile Gln His Gly  
35 40 45  
Trp Lys Glu Gly Asn Glu Pro Val Glu Gln Trp Lys Gly Thr Val Leu  
50 55 60  
Glu Gln Val Ser Val Lys Pro Thr Leu Tyr Ile Ile Lys Tyr Asp Gly  
65 70 75 80  
Lys Asp Ser Val Tyr Gly Leu Glu Leu His Arg Asp Lys Arg Val Leu  
85 90 95  
Ala Leu Glu Ile Leu Pro Glu Arg Val Pro Thr Pro Arg Ile Asp Ser  
100 105 110  
Arg Leu Ala Asp Ser Leu Ile Gly Lys Ala Val Glu His Val Phe Glu  
115 120 125  
Gly Glu His Gly Thr Lys Asp Glu Trp Lys Gly Met Val Leu Ala Arg  
130 135 140  
Ala Pro Val Met Asp Thr Trp Phe Tyr Ile Thr Tyr Glu Lys Asp Pro  
145 150 155 160  
Val Leu Tyr Met Tyr Thr Leu Leu Asp Asp Tyr Lys Asp Gly Asp Leu  
165 170 175  
Arg Ile Ile Pro Asp Ser Asn Tyr Tyr Phe Pro Thr Ala Glu Gln Glu  
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**PCT/US00/34960**

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449